

## Intensifying Multiphase Reactions and Reactors: Strategies and Examples

Utikar, R. P., & Ranade, V. V. (2017). Intensifying Multiphase Reactions and Reactors: Strategies and Examples. *ACS Sustainable Chemistry & Engineering*. <https://doi.org/10.1021/acssuschemeng.6b03017>

**Published in:**  
ACS Sustainable Chemistry & Engineering

**Document Version:**  
Peer reviewed version

**Queen's University Belfast - Research Portal:**  
[Link to publication record in Queen's University Belfast Research Portal](#)

### **Publisher rights**

© 2017 American Chemical Society.

This work is made available online in accordance with the publisher's policies. Please refer to any applicable terms of use of the publisher.

### **General rights**

Copyright for the publications made accessible via the Queen's University Belfast Research Portal is retained by the author(s) and / or other copyright owners and it is a condition of accessing these publications that users recognise and abide by the legal requirements associated with these rights.

### **Take down policy**

The Research Portal is Queen's institutional repository that provides access to Queen's research output. Every effort has been made to ensure that content in the Research Portal does not infringe any person's rights, or applicable UK laws. If you discover content in the Research Portal that you believe breaches copyright or violates any law, please contact [openaccess@qub.ac.uk](mailto:openaccess@qub.ac.uk).

# Intensifying Multiphase Reactions and Reactors: Strategies & Examples

Ranjeet P. Utikar<sup>1</sup> and Vivek V. Ranade<sup>2,\*</sup>

<sup>1</sup>Department of Chemical Engineering  
Curtin University  
GPO Box U1987, Perth WA 6845, Australia  
[r.utikar@curtin.edu.au](mailto:r.utikar@curtin.edu.au)

<sup>2</sup>School of Chemistry and Chemical Engineering  
Queen's University of Belfast  
Belfast BT9 5 AG, UK  
[V.Ranade@qub.ac.uk](mailto:V.Ranade@qub.ac.uk)

\* Corresponding author

## Abstract

Intensification is intrinsic to better chemical and process engineering and has always been used in practice. Multiphase reactions and reactors are ubiquitous in chemical and allied industries and are of great economic and ecological importance. There is a great scope for intensifying multiphase reactions and reactors for realizing productivity enhancements, which are crucial for sustainable manufacturing. These enhancements can be in terms of increased throughput; better yield, conversion, and selectivity; smaller environmental footprint; and intrinsically safer operations. The advances in intensified reactors especially micro-reactors and microfluidic devices have created significant awareness about intensification in recent decades. In this note, we discuss different strategies for intensifying multiphase reactions and reactors based on the published information. Variety of tools and examples are presented to showcase the potential of intensification. We have found the efforts towards intensification of multiphase reactions and reactors very rewarding academically as well as professionally. We hope that this note will further stimulate interest in this area and pave the way towards realizing next generation productivity for chemical and allied industries.

## Keywords:

Process intensification, multiphase reactors, micro-reactor, sustainable process development

## 1. Introduction

Chemical and allied industries are crucial for sustaining and enhancing quality of life as they touch lives of everyone, every day. The chemical industry faces its biggest challenges in rising raw material costs, depleting feedstocks, and stricter environmental regulations. These challenges also open up significant opportunities for innovation. It is essential to continuously focus on significant improvements in productivity via process innovations for conserving raw materials, catalysts, energy, and water. To enhance productivity, and thus economic impact, it is important that the chemical (and biological) transformations in a chemical process are carried out in the best possible way that is intrinsically safe and has smaller environmental footprint. A vast majority of such transformations involve multiphase reactions and reactors. Therefore, there is immense scope for intensifying multiphase reactions and reactors for realizing productivity enhancements.

Intensification may be broadly defined as the ability to obtain better results in terms of purity, conversion, and yield of the desired product by manipulating rates of relevant transport processes and chemical reactions so as to enhance overall performance (more throughput, better quality, less energy consumption, less waste, safer, etc.). This usually translates into a reduced cost, which has been the main driver behind intensification. It is therefore in a sense intrinsic to better chemical and process engineering and has always been used in practice. We were fortunate to get introduced to intensification very early in our research careers. Professor M M Sharma of UDCT (now called Institute of Chemical Technology, Mumbai) was one of the pioneers in intensifying multiphase reactions. He introduced one of us (VVR) to intensification and the benefits of it more than three decades ago (when process intensification had not become the buzz word as it is today). In his classic book [1] he has discussed several examples of intensification of multiphase reactions. In one of his papers with almost the same title as this note [2], he has discussed several examples of intensifying reactions. These works and the references cited therein are a must read for anyone interested in intensifying multiphase reactions.

Continuous improvement has been the cornerstone of the process industry and has resulted in significant advances in several process areas. For example, advances in materials and heat exchanger configurations have tremendously improved the energy efficiency of sulphuric acid plants over recent years. Compared to a traditional double catalyst double absorption process cycle, where almost 40% low level heat is wasted in acid cooling system, modern processes such as Monsanto Enviro-Chem's Heat Recovery System and Outokumpu's heat recovery system offer recovery of over 95 per cent of the process heat as steam. Recently, there has been significant effort to develop scalable technologies for the synthesis of carbon-neutral ammonia by conversion of intermittent energies (e.g., solar and wind) [3]. The new developments allow ammonia plants to behave like energy plants, a drastic shift from the traditional centralized, large scale, capital and energy intensive Haber-Bosch process.

In this note, we will focus on some of the recent work on intensification. Stankiewicz and Moulijn [4] have defined modern interpretation of process intensification as “the development of novel apparatuses and techniques that are expected to bring dramatic improvements in manufacturing and processing, substantially decreasing equipment size, energy consumption, or waste production, and ultimately resulting in cheaper, sustainable technologies”. The definition is still heavily biased towards new apparatuses and methods than on other avenues of intensification advocated by Sharma [2] and others. It also covers broader scope beyond chemical reactions. In this note, we will restrict the scope to intensification of chemical reactions and reactors. Intensification of other processes such as separations, unless they are intimately linked to reactions, is not included.

The advancement in intensified devices including microreactors and microfluidic devices has created significant hype and awareness about process intensification in recent decades. Nevertheless adoption of microdevices based technologies by industry is slow. Hundreds of research papers, many books and monographs are now available in this area. Owing to the continuous research, researchers and practicing engineers now better understand the limitations and strengths of process intensification technologies and continuous processing. As a consequence, more informed use and research plans for enhancing the adoption and relevant development of process intensification technology have emerged. There is a gradual but certain expansion of scope of research and development from microdevices to milli- or even centi- scale devices, which has considerably enhanced the potential for adoption in practice. Recently Ranade et al. [5] have described the development of MAGIC (modular, agile, intensified and continuous) reactors and their applications for intensifying variety of reactions. They have also discussed key drivers, factors, and tools available for intensifying reactions. Rather than focusing on such specific efforts on intensifying reactions, in this note, published studies on intensification of multiphase reactions and reactors are critically analyzed and useful strategies for intensification are extracted.

For any chemical reaction to occur, a reactor has to carry out several tasks such as bring reactants into intimate contact with each other as well as the active sites on catalyst, provide an appropriate environment (pressure, temperature, and concentration) for adequate time, and allow for timely removal of products. Naturally, successful reactor engineering requires bringing together better chemistry and better engineering. Better chemistry is achieved through understanding of thermodynamics, catalysis, and reaction pathways (Figure 1). Whereas, the engineering can be improved via insights into fluid dynamics, mixing, and heat and mass transfer, and real time process monitoring and control. Thus, it is important to combine the understanding of chemistry and catalysis with key reaction engineering expertise in order to realize true potential of intensification via following two avenues:

- Intensifying chemical reactions: this can be carried out in a variety of ways – improved catalysts (replace reagent based processes), better process routes, improved solvents (supercritical media, ionic liquids), better process windows (concentrations, temperature, pressure, etc.), improved atom efficiency, and alternative pathways to prevent waste;
- Intensifying transport processes – new ways of process intensification can come from improved underlying flows and associated transport processes (via experiments and computational models) to ensure that delivery of materials and energy at right time and right place at length and timescales which are appropriate to the reaction rather than driven by the process.

In the following section we briefly review published studies and attempt to capture key strategies for intensification. It should be mentioned here that major fraction of work on intensification realized in practice does not get published because of the proprietary and confidential nature of the work. Even the small fraction that gets published covers such a broad range that it is almost impossible to present an all-encompassing review in a single note. Naturally the emphasis on certain topics and the selection of examples is rather biased and is directly related to our own research interests and experience. We have, however, made an attempt to evolve general guidelines, which will be useful for generically addressing intensification of multiphase reactions/reactors. Some comments on path forward are also included at the end.

## **2. Strategies for intensification**

There are thousands of industrially relevant processes involving multiphase reactions. There are many books and resources, which highlight and cite many such reactions. For example, Doraiswamy and Sharma in their two-volume book [1] have listed hundreds (if not thousands) of reactions. Doraiswamy [6] in his treatise on organic synthesis engineering discussed many reactions. More recently, Joshi and Ranade [7] have listed several industrially relevant multiphase reactions in their edited book on industrial catalytic processes for fine and specialty chemicals. Instead of giving examples of such reactions here, reader is referred to these sources and references cited therein.

Multiphase reactions and reactors can be classified by variety of ways. One may classify these based on involved reactions like hydrogenations, oxidations, esterification, alkylation, halogenation, diazotization and so on. One may also classify these on more generic reaction types such as gas-liquid, liquid-liquid, gas-liquid-solid, liquid-solid, gas-solid and solid-solid reactions or reactor types such as stirred reactors, bubble column reactors, three phase fluidized beds, packed beds, fluidized beds, jet loop reactor, rotor-stator reactor, tubular reactors and so on. Significant efforts around the world continue to enhance and intensify the wide range of multiphase reactions and reactors. It is almost impossible to keep a track of all the published literature and critically review it. No such

attempt is made here. Instead, based on the limited and arguably biased exposure to the published and unpublished work which we are privy of is used to bring out key strategies of intensification.

As mentioned earlier, these strategies are broadly grouped into intensification of reactions and intensification of transport processes. Obviously the two strategies are not completely independent of each other. Any intensification strategy needs to first identify performance-limiting step and then make an attempt to eliminate those limitations. For example, if in a reactor rates of transport processes, such as mixing, are much higher than the reaction rate, intensification of reaction is an appropriate strategy. After intensification of underlying reaction, rates of transport processes may become limiting and intensification of transport processes may become an appropriate strategy. Intensification is thus a continuous activity and depending on relative rates of underlying reactions and transport processes at the time of consideration, appropriate strategy has to be selected. Key strategies used for intensifying reactions and reactors (transport processes) are briefly outlined in the following section.

Before we proceed to discuss strategies for intensification, it may be useful to highlight here that one of the best strategies for intensification of reactions is avoiding the reaction altogether! For example, consider a case of monochloroacetic acid (MCA) process. Conventionally, MCA is manufactured by chlorination of acetic acid in bubble columns or sectionalized bubble columns. This is an autocatalytic reaction and invariably some dichloroacetic acid (DCA) is formed in bubble columns or similar reactors. The DCA is converted to monochloroacetic acid by hydrogenation to avoid cumbersome and expensive fractional crystallization. The hydrogenation step can however be eliminated by using extractive distillation with suitable extractant [8]. Many other examples of similar nature can be identified. However, these are not considered in the present note. Other alternative to eliminate hydrogenation step or to reduce selectivity towards DCA is to use tubular milli reactors and control backmixing to such an extent that formation of DCA is within acceptable limit. Such intensification strategies are considered here.

## **2.1 Intensification of multiphase reactions**

One of the most obvious ways of intensifying reactions limited by intrinsic kinetics is to select an appropriate operating process window. For reactions of positive order, using higher temperature, reactant concentrations, and higher catalyst or promoter concentration wherever permissible, will lead to higher rates. One needs to be aware that intensification through this obvious route may lower selectivity towards desired product. The operating process window therefore needs to be optimized. There are several examples of such strategy in published literature and practice. For example, recently, Garkhedkar et al. [9] have reported significant intensification in effective reaction rate of hydrogenation of cinnamaldehyde to cinnamyl alcohol without

jeopardizing selectivity by appropriate selection of reactant concentration, catalyst and promoter concentrations, and hydrogen partial pressure. We don't discuss this strategy further in this note since it is commonly used even for single phase reactions. Instead, we focus our attention on three widely used strategies for intensifying multiphase reactions namely catalyst design, solvent design, and elimination of equilibrium limitations.

#### 2.1.1 Catalyst design:

Major advances and step changes for intensification of multiphase reactions will, no doubt, continue to emerge from catalysis. A catalyst provides an alternative route of reaction where the activation energy is lowered. Catalysts enhance rates of chemical reactions without affecting chemical equilibrium. Catalysts could be homogenous (catalyst and substrate in same phase) or heterogeneous catalysis (solid catalyst and substrate is a gas and/or liquid). Most of the homogeneously catalyzed systems also involve presence of immiscible phase and therefore are multiphase reactions.

The role of catalyst becomes significantly more important when multiple reactions are thermodynamically feasible. In such cases, appropriate catalyst manipulates the reaction rates in such a way that selectivity towards desired product increases. The catalyst performance is usually quantified using activity (rate of reaction), selectivity (towards desired product), and stability (deactivation, regeneration, reusability, life). With recent advances in molecular modeling, our understanding about atomic and molecular scale transformations around catalyst sites through which catalyst influences overall performance has improved significantly. It has enabled us to tailor catalysts for desired performance. In many cases, bi-functional catalysts are used to achieve desired selectivity. For example, Talwalkar et al. [10] used a bifunctional ion-exchange-resin catalyst for effective hydrogenation of diisobutylene (DIB). DIB is generally available as an equilibrium mixture of its isomers 2,4,4-trimethylpent-1-ene (TMP-1) and 2,4,4-trimethylpent-2-ene (TMP-2). The terminal double bond in TMP-1 gets hydrogenated substantially more quickly than the internal double bond in TMP-2, therefore, the isomerization of TMP-2 to TMP-1 is essential to achieve higher rates and yields of hydrogenation. The selectivity and effective rate was intensified using a catalyst that is active for hydrogenation as well as simultaneous isomerization.

The subject of catalyst design as a strategy to enhance multiphase reactions is very complex and broad. It is not possible to do a justice to the subject by including a short subsection in this note. Instead, we refer readers to Joshi and Ranade [7] and references cited therein for gaining deeper appreciation and advances in this area. We would like to mention here two different examples of catalyst designs for the purpose of illustration. The designing of "chiral" metal surfaces has significant potential and could form a basis for developing solid catalysts for region-specific chemistry (see review by Mallat et al. [11] for several examples and references on this subject).

Another example is of crystal lattice engineering to develop active and selective catalysts for converting biomass-derived polyols by Jin et al. [12]. Using this approach, a bimetallic nanocatalyst was designed by synthesizing copper-based nanocatalysts on reduced graphene oxide support. The catalytically active {111} facet was realized as the dominant surface by lattice-match engineering. It is hoped that such new methodologies for designing catalysts may open new vistas for exploiting graphene-based supports and improved metal-based catalysts for a variety of heterogeneous catalytic reactions. Yet another possibility of enhancing performance of catalyst is by designing appropriate supports for catalyst. Jin et al. [13] have designed heterogeneous support (TiO<sub>2</sub>) for bimetallic PtCu catalysts where the support is apparently acting as a “ligand” for the formation of nuclei, thus generating well dispersed Pt and Cu particles. They have demonstrated order of magnitude enhancement in oxidation activity with improved selectivity for catalytic synthesis of glucaric acid by oxidation of gluconic acid/glucose (using oxygen as oxidant). Creative and synergistic design of support and catalyst will open up new possibilities for developing greener and intensified processes.

#### 2.1.2 Solvent design:

Solvents are routinely used for carrying out reactions and influence not just the rates and productivity but also environmental impact. Solvents influence solubility of reactants, may interact with catalyst and may act as a heat carrier helping in providing heat for endothermic reactions or managing heat liberated in exothermic reactions. There is an increasing emphasis on identifying better solvents that offer higher productivity of reaction with lower environmental impact. Gadge and Bhanage [14] have recently reviewed selection of solvents and reaction media. They have discussed several options such as CO<sub>2</sub> expanded solvents, supercritical solvents (CO<sub>2</sub> and water), ionic liquids and so on.

In many applications it is beneficial to add a second immiscible solvent in the reaction system either to intensify reaction rate or to facilitate easy separation of catalyst/ products. Sharma and co-workers have demonstrated that addition of second immiscible liquid phase can significantly intensify rates of gas-liquid reactions. The second liquid phase has higher solubility for the gas and may be dispersed or emulsified. The additional phase provides extra mode of transport of the solute gas and thus enhances the rate. For example, Mehra [15] and Mehra et al. [16] report almost 30 times enhancement of the specific rates of alkaline hydrolysis of solid esters—2,4-dichlorophenyl benzoate, p-chlorophenyl benzoate and phenyl benzoate—in the presence of a second emulsified liquid phase (see figure 2a). In solid-liquid systems, Doraiswami and Sharma [1] and Sharma [2] have reported large enhancement in the rates of absorption of gases such as isobutylene, but-1-ene and propylene into emulsions of an additional liquid phase in aqueous sulfuric acid as well as microemulsions/ micellar solutions. Thus addition of second immiscible liquid can be effectively used for intensifying large variety of multiphase reactions.



An example of solvent design to derive the benefits of high activity homogeneous catalyst without the associated difficulties of separation of homogeneous catalyst is to use a thermomorphic solvent (TMS) system. A TMS consists of at least two solvents with different polarity [17]. As shown in Figure 2b, the solvents are immiscible at low temperature and form a single homogeneous reaction phase at higher temperatures. An appropriate system can be chosen such that the catalyst is predominantly soluble in one solvent and the other solvent has higher affinity towards the product. Dreimann et al. [18] have reported selection of TMS system for hydroformylation reactions to reduce the difficulties in downstream separation significantly.

Other interesting way of intensifying multiphase reactions is by selecting appropriate solvent that allows efficient removal of heat liberated due to reactions and eliminates heat transfer limitations to increase effective rate. For example, Deshpande and Dixit [19] disclose new process for polyolefins where polymerization occurs in a suspended phase, which allows viscosity to remain within limits and provides effective mixing and heat transfer. Use of acetic acid for oxidation of para-xylene is a well-known example of effectively using evaporation of solvent for removing heat of reaction. Recently Ranade et al. [20] have disclosed a way of intensifying hydrogenation of nitrobenzene via use of evaporating solvent.

While the use of solvents offers advantages, they effectively reduce reactant concentration and may reduce productivity of reactor if the reactor is operating under kinetically limiting conditions. In such case, alternative ways of carrying out the reaction with minimal or no solvents can be explored. Grinding of solid reactants is emerging as an alternative to conventional solvent-intensive methods. James et al. [21] provide a critical review of mechanochemical synthesis. Recently order(s) of magnitude higher space time yields over conventional methods have been reported by using screw extruders (Figure 2c) for the continuous synthesis of various metal complexes, including metal organic frameworks (MOFs) [22,23].

#### *2.1.3 Overcoming equilibrium limitations by combining reaction and separation:*

Many reactions used in practice are reversible in nature and often the conversion is limited by thermodynamic equilibrium considerations. Integration of possible ways of removing one of the products from the reacting mass is often the way to intensify such reactions. Distillation, chromatography and membrane separations are the most studied separation processes integrated with reactors to facilitate in-situ product removal for shifting reaction equilibrium in forward direction. Recently Reddy et al. [24] compared two multifunctional reactors, reactive distillation and chromatographic reactors, for the production of C1–C4 carboxylic esters. There are several examples of reactive distillation including the celebrated methyl acetate process by Eastman [4]. Stripping is used for removal of products and intensification of urea alcoholysis reactions in dialkyl carbonates

process [25,26]. Fernandez et al. [27] have shown that use of membrane reactor can significantly enhance conversion and purity of produced hydrogen for methane reforming reaction. Membrane reactors have also been shown to be useful in intensifying bio-transformations and enhancing selectivity [28, 29]. These examples provide useful guidelines for intensifying equilibrium limited multiphase reactions and reactors.

## **2.2 Intensifying multiphase reactors**

Several factors influence overall performance of a multiphase reactor. Extent of backmixing (from completely mixed to a plug flow) in the reactor, mode of operation (batch, semi-batch, and continuous), and reactor configuration (single versus multiple) influence reactor performance for single as well as multiphase systems. Specific strategies that are relevant for intensifying multiphase reactors are discussed here. Obvious strategies such as changing reactor configuration, which are generic in nature are not discussed. For example, recently Atias et al. [30] disclosed use of two reactor configuration for epoxidation. Epoxidation involves two steps: etherification and dehalohydrogenation (epoxidation). Unlike conventional process, where, both the steps take place in the same reactor, intensification is achieved by splitting the reaction into two reactors [30]. They further intensify the liquid-liquid epoxidation step by using a high shear mixer for carrying out the epoxidation step. The strategies like carrying out the reaction into two reactors which is generic and useful for homogeneous reactions are not discussed here. However, the strategies like using high shear mixer for intensifying liquid – liquid epoxidation reaction will be discussed in the following. Here we discuss the intensification of multiphase reactors by the following three strategies: intensifying mixing, heat transfer, and mass transfer.

### **2.2.1 Intensification of mixing:**

There are several ways to intensify mixing controlled reactions. Most of these efforts are directed towards reducing characteristic length scales of diffusion and mixing. For turbulent flows, it is achieved by enhancing and concentrating turbulent energy dissipation rates. For laminar flows, the length scales are usually reduced by realizing folding and refolding of lamellar structure and reducing thickness of lamellas. Some of the augmentation of mixing and other transport processes are summarized by Ranade et al. [5]. Variety of high shear mixers using rotor-stator flows can be used for intensifying micro-mixing controlled reactions (such as polyurethane reactions). A large number of innovative designs of static mixers have also been developed for intensifying mixing controlled reactions. Besides these conventional ways of intensifying, many new ideas have been proposed and used to intensify mixing.

Novel micro-mixers have been proposed for realizing faster mixing in laminar flows [31,32]. Recently Boroun and Larachi [33] proposed use of magnetic nanofluid actuation by rotating magnetic fields for intensifying liquid mixing. They have shown that mixing index can be tripled compared to that obtained without magnetic field.

Boroun and Larachi [34] have also discussed a possibility of tailoring the physical chemistry of magnetic nanoparticles (MNPs) for enhancing transport rates. In future, it may be possible to use bifunctional magnetic nanomaterials which simultaneously carry out catalysis as well as intensify local mixing.

#### *2.2.2 Intensify heat transfer:*

Many reactions used in practice are highly exothermic and often the ability to remove heat liberated from reactions controls the achievable productivity. Many times such exothermic reactions are deliberately carried out at low temperatures (at low reaction rates) to match rate of heat liberation with rate of heat removal. Enhancing heat removal capacity, mainly by significantly enhancing heat transfer area may intensify such reactors. Heat transfer area per unit volume of reactor is inversely related to the characteristic length scale of reactor cross-section. Most of the process intensification efforts are focused on devising new reactor types having smaller characteristic length scales. By reducing the characteristic length scales of heat transfer channels to around 0.01 m and less, the heat removal capacity can be enhanced to 1000 kW/m<sup>3</sup>. The obvious choice of reactors for systems requiring such large heat removal capacity is therefore tubular (topologically) reactors. Several designs of such topologically tubular reactors have been proposed.

One of the simplest designs is pinched tube disclosed by Kulkarni and Ranade [35] (Figure 4b). Pinched tubes have shown to offer enhanced heat transfer and reduced axial dispersion which make them suitable for carrying out exothermic reactions [36, 37, 38]. Joshi et al. [39] have demonstrated safe operations with several multiphase exothermic reactions using pinched tube reactors. Andersson et al. [40] have developed novel intensified reactor for liquid-liquid reactions that has eventually lead to compact plate heat - exchanger cum reactor from Alfa Laval. Such strategies can be used to intensify heat transfer limited multiphase reactions and reactors.

#### *2.2.3 Intensify mass transfer:*

Many multiphase reactions are limited by mass transfer. For different multiphase reactors, different intensification strategies for mass transfer are required. Generically these involve reducing diffusion time scales and enhancing mass transfer area. For example, one of the ways of intensifying gas-liquid-solid reactions in trickle bed reactors is use of in-line monolithic reactor [41]. Here the catalytic reactor is not a separate vessel but is an integral part of the pipeline in the form of wash-coated monolith in which the reaction between the pre-dispersed gas and the liquid takes place. A significant reduction of the equipment size can be achieved due to much greater catalytic effectiveness in the wash-coated monoliths compared to convention trickle beds.

Pollington et al. [42] demonstrate continuous flow structured reactors for the oxidation of glycerol under mild conditions using a gold/carbon catalyst. Compared to autoclave studies, monolith and mesoscale structured

down-flow slurry bubble column designs lead to one and two orders of magnitude enhancement in the reaction rate respectively. The monolith reactor offers structured contact of gas-liquid-and solid reacting phases that results into enhanced interaction between bubbles and particles compared to a thin channel slurry bubble column where the solid phase is allowed to freely move within the channel. Consequently, much higher selectivity to glyceric acid is observed in the monolith reactor compared to the thin channel slurry bubble column.

Several well known catalytic reactions such as hydrogenation, Fischer Tropsch synthesis, oxidation etc. have been carried out in micro packed-bed reactors. Pennemann and Kolb [43] present a review on the operation of microstructured reactors for selective oxidation reactions. Faridkhou et al [44] present an overview of mass transfer and hydrodynamics in micro-packed beds.

For gas-liquid reactions, smaller bubbles can substantially improve gas-liquid mass transfer. For example, in a new type of static mixing element [45,46] screens/grids are used to obtain interfacial areas as high as  $2200 \text{ m}^2/\text{m}^3$  (compared to  $200 - 400 \text{ m}^2/\text{m}^3$  in bubble column). These screens have also shown to be very effective in promoting liquid – liquid mass transfer and reached values greater than  $4 \text{ s}^{-1}$  at low specific energy consumption rates. Similar concept is also proposed [47,48] for generating smaller bubbles in bubble columns.

Using small channel reactors, Enache et al. [49] demonstrate intensification of homogeneously catalyzed gas–liquid reactions. Solvent-free hydroformylation of cyclododecatriene using a homogeneous catalyst carried out in a heat-exchange (HEX) reactor with millimeter scale thin channels is shown to be order of magnitude faster than that in a stirred batch autoclave. Operation in the HEX reactor eliminates mass transfer limitations and the observed turnover frequency is independent of catalyst concentration. On the contrary, the catalyst productivity in the autoclave is a function of its concentration indicating mass transfer limitations. The selectivity to the desired monoaldehyde product is also higher in the HEX reactor.

Metal-catalyzed gas–liquid reactions such as hydrogenation, carbonylation and hydroformylation are ubiquitous in pharmaceutical and fine chemical production. Typical gas– liquid reactions are performed in stirred batch reactors, where the gaseous reactant is pressurized in the headspace above the stirred liquid phase containing the substrates and catalysts, and are often hindered by heat and mass transport limitations due to low specific interfacial areas. Such limitations can be mitigated through the use of micro-/milli-reactors as platforms for multiphase organic syntheses due to the tremendous transport acceleration inherent in these small scale flowing systems. A triphasic segmented flow milli reactor is reported [50,51] for intensifying metal catalyzed gas–liquid reactions. Despite the involvement of an additional immiscible fluid phase wherein catalysts are ‘immobilized’, the pseudo-biphasic reaction system is able to provide significant enhancement in mass transport. This results

in higher yield and selectivity with residence time of a few minutes. The approach can be extended to other similar catalytic reactions, incorporating both homogeneous and heterogeneous catalysts.

### **3. Tools and examples of intensification of multiphase reactions/ reactors**

The strategies discussed in the previous section are quite intuitive and are often discussed in textbooks. There are variety of tactics and tools, which can be used to implement these strategies successfully in practice. We have cited some of the tools and examples while describing these strategies. In this section, additional discussion on tools with examples is included. Considering the vast scope and wide variety of multiphase reactions/ reactors, obviously only a small fraction of such tools/ examples can be discussed here. We hope that discussion conveys the general flavor and provides useful pointers for wider applications. The discussion is organized along the lines of different tools/ tactics which may be useful for implementing multiple strategies discussed in the previous section. Emphasize is on intensification of multiphase reactions/ reactors via transport processes or operating window rather than on catalyst and solvent design.

#### **3.1 Topologically tubular reactors and continuous processing**

In recent years, there is a significant push in fine and specialty chemicals sector to convert batch processes to continuous processes using small topologically tubular reactors offering substantially higher mixing, heat and mass transfer rates. Many books and monographs on this area have been published besides hundreds of research papers. Several research institutes and universities throughout the world have programs based on continuous flow synthesis and manufacturing at various levels. Recently Ranade et al. [5] have highlighted the use of topologically tubular reactors (so called MAGIC tubes) with mm or cm scale characteristic dimensions. Different possible ways of augmenting mixing and transport rates of such tubular reactions were also discussed. Simple idea like pinching of tubes have been shown to improve mixing and heat/ mass transfer. Pinched tube reactors and AmAR reactors [35] have been extensively used for intensifying several multiphase reactions including nitration [52] and diazotization [53]. These MAGIC tubes derived from commercially available tubing can significantly reduce the cost of manufacturing while retaining major advantages offered by narrow channel reactors.

Joshi et al. [39] have demonstrated the use of tubular reactors for very efficient synthesis of a large family of beta amino crotonates. The higher heat and mass transfer rates offered by the tubular reactors allows reactions at much higher temperatures compared to conventional semi-batch reactors. This results in orders of magnitude reduction in required residence time compared to the batch time required with semi-batch system. Kulkarni and co-workers have developed continuous-flow nitrations using fuming nitric acid. For example, Sharma et al. [52] present intensification of nitration of o-xylene with only fuming nitric acid as the nitrating agent. They

demonstrate use of multi-section reactor comprising tubes of different diameters for different section is more economical than a reactor comprising a single tube size.

Tonkovich and Deshmukh [54] have intensified hydrocracking process for conversion of solid wax (typically C<sub>20</sub>+ fraction of the FT hydrocarbon product, produced in a Velocys microchannel reactor) to produce diesel and other liquid fuel products. Process intensification was demonstrated with an order of magnitude increase in catalyst productivity, 10 to 30 hr<sup>-1</sup> WHSV. The flow regime of the gas-liquid interaction was tailored to the meet the requirements of thin liquid film and enhanced productivity per unit catalyst weight. Despite the high WHSV, complete conversion of the solid hydrocarbon fraction was obtained and varying the feed WHSV is shown to have an influence on the final fuel product. Operating conditions can be carefully selected to obtain a tailored fuel product.

The application of various reaction conditions in micro-reactors using segmented flow can dramatically increase the reaction rates for a simple biphasic hydrolysis [55]. The approach is effective in intensifying homogeneous reactions such as diazotation/ Heck reaction as well. Continuous processing is also found to be effective in intensifying photochemical reactions relevant to organic synthesis, materials and water treatment [56].

Damm et al. [57] show high-temperature continuous-flow synthesis of adipic acid from cyclohexene, cyclohexanol and cyclohexanone using aqueous H<sub>2</sub>O<sub>2</sub> and tungstic acid as catalyst without using any phase transfer catalysts (PTCs). Absence of PTC greatly simplifies downstream processing. The intensified process based on H<sub>2</sub>O<sub>2</sub> potentially offers an attractive way of manufacturing adipic acid without N<sub>2</sub>O emissions (as in conventional process). Oxidation using air or oxygen are often limited by mass transfer effects which can adversely affect reaction kinetics and selectivity, or lead to irreversible decomposition of a catalyst. There is also a possibility of formation of flammable mixtures of oxygen and solvent vapor. Therefore despite showing versatility and promise on a laboratory scale, these aerobic oxidations are not widely used in specialty chemicals and pharmaceutical sector. Recent advances in continuous processes using small diameter tube- or plate-reactors are expected to change this. Gutman et al. [58] developed a continuous flow N-demethylation with molecular oxygen as oxidant. The catalytic oxidative demethylation with molecular oxygen offers an atom-economic and environmentally benign alternative to traditional procedures. Gemoets et al. [59] have reviewed continuous-flow liquid phase oxidation chemistry in microreactors using oxygen, hydrogen peroxide, ozone and other oxidants. Relevant mass and heat transfer phenomena are discussed to facilitate judicious choice for a suitable reactor. Besides the safety aspects, the scale-up potential is also described. Erdmann et al. [60] report the first continuous cross-dehydrogenative homocoupling of an unactivated arene using oxygen as sole oxidant.

Use of microreactor technology enables operations at elevated temperatures and pressures with significant reduction in required residence time [61].

Peer et al. [62] report intensification of biphasic alcohol oxidation with hydrogen peroxide using solvent free continuous reactor with in-line separation of the tungsten polyoxometalate catalyst and phase transfer catalyst from the product. Zinc-substituted polyoxotungstate in combination with the selected phase transfer catalyst drives the oxidation reaction to completion within a short residence time (5–10 min). Corning flow reactors with in-line membrane-based liquid–liquid extraction units at the reactor outlet is used for scale up. A three-stage countercurrent liquid–liquid extraction system is used for removing most of the phase transfer catalyst from the desired organic effluent stream while reducing the amount of extraction solvent required.

Jeong et al. [63] have intensified transformation of natural lignocellulosic biomass resources by developing an integrated continuous two-step microfluidic system as a platform for direct conversion of fructose to diverse furan chemicals with excellent yields. A sequential two-step process is utilized to complete the dehydration of fructose in the surface acid catalyst followed by the four types of HMF conversion in a binary or ternary phase with magnetic-based heterogeneous catalysts using residence time of few min to 1 hr. This transformation platform was extended to ternary oxidation and hydrogenolysis reactions in the tube-in-tube system for the production of DFF and DMF. In particular, the supported catalysts on the magnetic Fe<sub>3</sub>O<sub>4</sub> particles enabled easy positioning of an appropriate amount of catalyst at the inner wall of the microchannel using an external magnet. This approach appears to be promising for transforming natural lignocellulosic biomass resources to meet industrial requirements.

Heitmann [64] have presented process intensification work at Clariant and highlighted that the work has enabled design of modular container-based (pilot) plant for intensified continuous production processes. A flexible modular container plant is currently engineered for performing amidation and esterification reactions. Modular container plants can create opportunities to change the way of thinking about new processes and new production facilities besides offering advantages in terms of safety, efficiency, and product quality.

Continuous reactors have also facilitated intensified and safe production of hazardous reactions and reagents. Singh et al. [65] have developed a continuous zero exposure system for chloromethyl methyl ether chemistry involving carcinogenic reagent. It relies on a novel membrane-free SiNWs microseparator to allow for the separation of low boiling chemicals by simple heating in a continuous-flow manner. This total process concept including the integrated system and procedure can be easily extended to other carcinogenic, explosive, toxic or noxious reagents. Movsisyan et al. [66] report recent examples of hazardous reactions successfully carried out in

continuous flow reactors. As demonstrated in this review, new advances in reactor technology make hazardous chemistry accessible.

Karande et al. [67] review microreactors for biocatalytic applications. During the past decade, there is a rapid rise in integrating microfluidic reactors and biocatalytic reactions for various applications. The combination of miniaturized technologies and microfluidics allows coupling of scale- and time dependent phenomena for bioprocess intensification. Dimensionless numbers are discussed, which help identify rate limiting steps and offer opportunities to enhance the overall reaction performance in solid-liquid biocatalytic reactions. This integrated concept is realized in a case study based on the biocatalytic conversion of styrene to (S)-styrene oxide using catalytic biofilms.

It is of course possible to intensify multiphase reactors by converting batch mode to continuous mode even without using tubular reactors. For example, Van Alsten et al. [68] have intensified hydrogenation reactor by making it continuous using two stirred tank reactors in series. A dinitro intermediate in a smoking cessation drug, is reduced in a two-reactor continuous stirred tank train to the diamine product. The two reactors operate within different regimes: the upstream reactor exhibits hydrogen mass transfer limited behavior, and the downstream reactor shows substrate concentration limited behavior. By manipulating reaction conditions in the two continuous reactors (catalyst, temperature, and substrate concentration), significant improvement over conventional batch processing are achieved. Recently Rode et al. [69] have converted batch hydrogenation of nitrobenzene to para amino phenol to continuous process with significant enhancement in productivity.

### 3.2 Interphase transport rates

It is obvious that enhancing interphase contact will improve transport rates and therefore intensify multiphase reactions/ reactors. Several different ways and ideas have been developed for intensifying interphase contacts. This may include reduction in characteristic dimensions, enhancing local energy dissipation rates, use of spatially or temporally periodic flows etc. It must however be mentioned here that intensifying mass transfer will not necessarily lead to performance enhancement all the time. Sometimes you may need an optimal value of mass transfer to get better selectivity.

This is illustrated by the example discussed by Lohokare et al. [70]. In this example, the liquid phase reactant (A) is hydrogenated in the presence of a catalyst to give partially hydrogenated liquid phase molecules of B and completely hydrogenated molecule C. B is the desired product. The selectivity towards B was maximized by operating the reactor in a mass transfer controlled regime by realizing appropriately low value of mass transfer coefficients ( $k_L a$ ). Intensifying mass transfer in this case will lower selectivity towards B. The optimal value of



mass transfer coefficient was realized by using external loop gas lift reactor which can keep catalyst suspended at lower values of gas superficial velocity (and therefore at lower values of gas-liquid mass transfer coefficient) than conventionally used stirred or bubble column slurry reactor.

There are of course several cases, where intensifying mass transfer or heat will enhance reaction/ reactor performance. Some ideas for realizing such enhancement in transport rates are discussed in Section 2.2. Some more examples and tools are discussed here. One of the ways of intensifying multiphase reactions/ reactors is separating reaction and mass transfer step and use independent intensifying strategies for these two operations. For example, Otterstatter et al. [71] have used an absorber – fixed bed reactor combination for intensifying oxidative esterification. Instead of relying on gas-liquid mass transfer in trickle bed reactor, external absorber was used to contact gas and liquid. Similarly Tan et al. [72] have intensified catalytic hydrogenation of ethylanthraquinone by passing the gas-liquid microdispersion system through a packed bed reactor. Two orders of magnitude larger values of the overall volume mass transfer coefficient (compared to the conventional trickle bed reactors) were achieved in the microdispersion reaction system.

Another way of intensifying gas-liquid reactions is instead of sparging gas into liquid phase, one can significantly enhance gas-liquid mass transfer by spraying liquid droplets into gas phase. Subramanian et al. [73] have disclosed such a spray reactor for selective oxidation process. This involves introducing small droplets of liquid reaction mixture having oxidizable reactant, catalyst, and solvent into a reaction zone containing oxygen and diluent gas at a suitable reaction temperature and pressure.

Several other new types of reactors have been proposed to intensify transport rates and therefore multiphase reactions/ reactors. Some of these such as monolith reactors and topologically tubular reactors are mentioned earlier. Grasemann et al. [74] reported a modified bubble column staged by structured catalytic layers with integrated crossflow micro-heat-exchangers (HEX) (figure 4d). The HEX integrated within a staged bubble column reactor (SBCR) with catalytic layers made of Pd/ZnO on sintered metal fibers showed a high specific productivity in the solvent free hydrogenation of 2-methyl-3-buten-2-ol. Despite the observed influence of external mass transfer on the overall catalyst performance, the SBCR productivity was several orders of magnitude above the values obtainable in conventional reactors.

Rehm et al. [75] developed a microstructured falling film reactor for the dye-sensitized photochemical conversion of 1,5-dihydroxynaphthalene to juglone. This continuous-flow microreactor enables the efficient contacting of a gas and a liquid phase in combination with external irradiation by high-power LED arrays. Two sensitizers were used for the photochemical in situ generation of singlet oxygen as key step in the synthesis of the natural product

1 juglone. The dye-sensitized activation of molecular oxygen offers an important strategy to incorporate oxygen  
2 into molecules under mild reaction conditions. The intensified gas-liquid contacting and uniform irradiation  
3 offered by falling film reactor offer an attractive way to implement this in practice. Use of thin plate photo  
4 reactors (rectangular chambers illuminated from both sides) have yielded significantly higher productivity of  
5 microalgae compared to conventional shallow raceway ponds. Possible synchronization among random cell  
6 motion, the intrinsic rate-limiting steps for photosynthesis, and the time scale for photon harvesting may allow  
7 further possible enhancement in productivity of such thin photobioreactors [76].

8  
9 Several new reactors concepts such as three levels of porosity reactor (Figure 3a) have been proposed for  
10 intensification of multiphase reactions/ reactors. Introducing new reactor concepts in process industries is a  
11 lengthy process. Industry is reluctant to introduce novel chemical reactor types in existing processes when  
12 replacement is not essential. Many of the new reactor concepts therefore remain at the laboratory scale. Besides  
13 the topologically tubular reactors and their different versions as Amar Reactors mentioned earlier, there are  
14 many new concepts relying on rotating components. These reactors essentially rely on centrifugal forces for  
15 intensifying transport rates. Visscher et al. [77] provide a review of the current state-of-the-art in the field of  
16 rotating reactors. Their main advantages and disadvantages are presented, including the typical operational  
17 conditions (residence time, rotational speed, energy consumption).

18  
19 The rotor-stator spinning disc reactor (rs-SDR, Figure 4a) is one such multiphase reactor which aims to intensify  
20 transport processes by applying centrifugal forces and high-shear conditions. It combines the features of a  
21 classical spinning disk with a liquid film on the rotor [78] and those of a rotor-stator spinning disk reactor [79].  
22 In this new configuration, gas and liquid are co-fed through an inlet in the top stator. It is shown that gas-liquid  
23 mass transfer mainly takes place in the dispersed region between the rotor and the bottom stator and the  
24 volumetric mass transfer rate is up to a factor of 6 larger than in the region with the liquid film on the rotor. This  
25 reactor has a good potential for scaling up: gas and liquid can be co-fed from one rotor-stator unit to another  
26 without the need for redistribution of the gas.

27  
28 Subramanian et al. [80] and Harting et al [81] discuss inclined rotating fixed bed reactor for process intensification  
29 of heterogeneous catalytic multiphase reactions. The basic idea of the new concept is to superimpose reactor  
30 inclination and rotation. The superimposed rotation of the inclined reactor results in a catalyst wetting  
31 intermittency through periodic immersion of the catalyst packing into the accumulated liquid phase. Several  
32 advantages such as periodic refreshment of the liquid at the catalyst surface and product removal, efficient  
33 transfer of the reaction heat to the liquid, improved access and transfer of the gas phase to the drained catalyst  
34 section and less crucial role of the gas-liquid distributor due to forced flow pattern may be foreseen. DASHILBORUN

et al [82] present a low shear rotating reactor concept that promises more flexible adjustment of pressure drop, liquid saturation, liquid residence time, and back-mixing at constant flow rates. The implementation of the reactor concept will however increase complexity of operation and will require significant additional investments. The additional complexity and costs have to be counterbalanced by enhanced performance.

One of the other strategies proposed for enhancing transport rates in trickle bed reactors is use of periodic flows. Dietrich et al. [83] have recently shown that performance of trickle bed reactor for reactions limited by the mass transfer of the gaseous reactant can be improved by the modulation of the hydrodynamics. It was recommended to realize higher proportion of the void channels with vigorously fluctuating values of the liquid hold-up for intensifying performance. It is also possible to use spatially non-uniform distribution instead of temporally non-uniform distribution of liquid to realize similar intensification. Care has to be taken however to ensure that macroscale maldistribution does not arise in the process. They have reported more than 150% enhancement in reaction rates via this strategy. Gelhausen et al. [84] further modified this concept by proposing a novel concept, referred to as the 'Siphon Reactor' (Figure 3b). This reactor comprises a fixed catalyst bed in a siphoned reservoir, which is periodically filled and emptied. This serves to alternate liquid-solid and then gas-liquid mass transfer processes. By manipulating the duration of each phase, mass transfer can be harmonized with the reaction. Residence time experiments demonstrate that, in contrast to periodically operated trickle-bed reactors, the static liquid hold-up is exchanged frequently and uniformly due to the complete homogeneous liquid wetting. Periodic operation have also been suggested for intensifying other reactions/ reactors. For example, Nikolic et al. [85] have shown that periodic operation with modulation of inlet concentration and flow rate for improving reactor performance. They have illustrated this with an example of hydrolysis reaction of acetic anhydride.

Trickle beds also suffer from plugging by fine particles in liquid feed. Hamidipour and Larachi [86] developed a strategy based on modulation of electrical conductivity in kaolin/kerosene suspensions for countering plugging of trickle bed reactors / hydrotreaters. The suspension stability was remarkably enhanced through ON-OFF concentration modulation of an electrolyte-based kerosene conductivity improver and resulted in an efficient bed-cleaning strategy under operating conditions. Periodic additions of the conductivity improver enabled fines and deposits to gain momentarily large and similar electrical charges undoing, or impeding, multilayer deposition. The strategy was shown to be effective in mitigating deposition and in preventing filtration-induced flow maldistribution

One may also think of providing a non-stochastic microreactor alternative to the conventional trickle-bed reactor. Liedtke et al. [87] have demonstrated the enhancement in solid-liquid mass transfer in small diameter segmented flow reactors (Figure 3c). They demonstrate that slug length and particle size (as long as particles are

bigger than 50  $\mu\text{m}$ ) have no influence on mass transfer. The mass transfer coefficient depends mainly on overall flow velocity and an adequate circulation of solid particles in the liquid phase. For well suspended particles, higher Sherwood numbers up to 8.75 could be realized. For gas-liquid systems where reactor could be operated at higher two phase velocities, Sherwood numbers up to 15 were obtained. Losey et al. [88] could increase the overall mass transfer coefficient for gas-liquid absorption by more than two orders of magnitude (compared with values reported for traditional multiphase packed-bed reactors) by using a microfabricated packed-bed reactor consisting of 10 channels loaded with catalyst particles.

### 3.3 Alternative energy sources

For many multiphase reactions/ reactors heating contributes significantly towards process heating requirements. Consequently, minimizing waste heat losses as well as recovery and use of waste heat provide an avenue for intensification. Alternatively, instead of heating the environment, delivering the energy directly where it is required improves energy efficiency significantly. Use of selective heating techniques like alternating electromagnetic fields at different operating frequencies (microwave, ultraviolet, plasma, ultrasound), acoustic and hydrodynamic cavitation, magnetic fields, and high gravity fields, has been identified as a key approach for process intensification [89]. Stefanidis and Stankiewicz [90] give a broad overview of alternative energy sources for process intensification. While there are a few examples of commercialization of alternate energy sources [91], widespread industrial adoption of these energy sources closely depends on the robustness, safety, flexibility, and capital and operating costs. Here we discuss a few key examples.

Heating techniques such as microwave, ultraviolet, and other electromagnetic processing methods deliver more useful heat to the product reducing waste. They also offer control of additional process parameters such as the electromagnetic frequency, energy input, and spatial extent making them more flexible. As the interaction of electromagnetic energy with matter varies from material to material, electromagnetic processing techniques can enable entirely new or enhanced manufactured products and have been widely employed in chemistry as an energy source. Ramírez et al. [92] describe ethylene epoxidation in microwave heated structured reactors. They use catalyst that also acts as a MW susceptor. By rapid selective heating the catalyst, significant energy savings can be achieved. Benaskar et al. [93] give a cost analysis of production of 2-acetoxybenzoic acid as aspirin and 4-phenoxy pyridine as antibiotic precursor in Vancocin production using a combination of microprocessing and microwave heating. They emphasize the need to approach process-design in a holistic manner rather than focusing only on the reaction. The advent of tailored magnetic nanoparticles (MNP) has opened a whole new avenue of exploiting magnetism for intensifying multiphase reactions and reactors. Boroun and Larachi [34] list down various opportunities and challenges in utilizing MNPs for intensification. Cravatto et al. [94] describe use of sound energy for intensifying catalytic reactions in water: assisted by ultrasound and/or hydrodynamic

cavitation. Cavitation implosion generates mechanical and chemical effects such as cleaning of catalyst surface and formation of free radicals by sonolysis of water. They present overview of sonochemical reactions in water (oxidation, bromination, aza-Michael, C–C couplings, MCR and aldol reactions) for furthering the progress of organic synthesis using harmless and greener sound energy. Chakma and Moholkar [95] have demonstrated intensification of degradation of azo and non-azo dyes using sonochemical methods. Gaikwad and Gogate [96] demonstrated use of ultrasound assisted production of biodiesel using heterogeneous catalysts. Dubey and Gogate [97] reported ultrasound assisted selective O-Alkylation of Vanillin with Benzyl Chloride to form 4-Benzyloxy-3-methoxybenzaldehyde. The work has clearly established a superior process for synthesis based on the use of ultrasonic irradiations with higher yields as compared to the conventional approach. Ranade et al. [98] disclose a hydrodynamic cavitation device based on vortex diode for wide range of effluent treatment applications (figure 4c).

The use of alternative energy sources for intensification will find increasing applications in the coming years. It is important philosophically to think about possible ways of harnessing low entropy energy sources like electricity for enhancing selectivity towards the desired product. Electrochemical technologies and processes are still relatively untapped despite the successes for large processes like chlor-alkali and aluminium. Developments in electrochemical synthesis and methods in last couple of decades are expected to open up new opportunities for intensified electrochemical manufacturing of chemicals [99].

### 3.4 Computational modelling

Computational modelling can make significant contributions towards realizing potential intensification of multiphase reactions/ reactors. These computational tools may range from molecular modelling on one hand (for design and optimization of catalysts) to life cycle analysis tools on the other hand (for selecting appropriate process routes) with reactor engineering models and computational flow models (CFM) as intermediate levels. CFM is being increasingly used for intensifying multiphase reactions/ reactors. Role of computational flow modelling for enhancing reactor performance has been discussed extensively by Ranade [100]. Some examples of using chemical reaction engineering as well as computational flow modelling for intensifying multiphase reactions/ reactors are briefly mentioned here to illustrate the potential of this tool.

Computational models have been extensively used for enhancing intensification of fixed bed reactors. These may range from using reaction engineering models to intensify reactions or regeneration of fixed bed reactors to using computational fluid dynamics (CFD) based models of flow, heat transfer and reactions around catalyst pellets to optimize shapes and sizes of pellets. For example, Hou et al. [101] used computational models and used these for optimization of packed bed reactor carrying out the Sabatier reaction system. They obtained

significant reduction in bed length (220 mm to 150 mm) and pressure drop (2.62 kPa to 1.64 kPa) for the same hydrogen conversion by designing a concurrent preheating using the model. This reflected significant advantages considering space applications of this reaction. Girotra and Ranade [102] used relatively simple models to intensify low temperature regeneration of coked fixed bed reactor. The coked reactors are usually regenerated by gasification using air or oxygen mixed with diluents like steam, nitrogen or carbon dioxide. Because of exothermic coke combustion reaction, temperature rise in the reactor is of primary concern. Girotra and Ranade [102] used the computational models to develop optimal regeneration protocols which will minimize regeneration time (down time from the manufacturing perspective) and energy requirements.

CFD models have been extensively used for eliminating maldistribution in fixed bed reactors. For example, Ranade [103] have used CFD model to minimize mal-distribution by designing variable resistance support plates for radial flow fixed bed reactor for isomerization. Unlike the bed scale models, particle resolved CFD simulations, where flow around individual particle is simulated, can provide insights into interactions of heat and mass transfer with chemical reactions occurring on catalyst surface. Dixon et al. [104], Wehinger et al. [105] and Karthik and Buwa [106] used particle resolved CFD models for understanding and improving reforming reactors. While these simulations are computationally intensive, they provide insights that can be harnessed for intensification.

Performance of fluidized bed reactors have been significantly enhanced using CFD models. For example, Ranade [107] used multiple computational models to re-design spargers and internals for regenerators of fluid catalytic cracking (FCC) reactors to intensify regeneration process. Similarly Nayak et al. [108] demonstrate the use of CFD models to design improved oil injection nozzles in FCC reactors. CFD models were also shown to significantly enhance throughput of fluidized bed oxy-chlorination reactors by improving mixing and sparger grid design [109]. Lu et al. [110] have shown that multi-scale CFD models could be used to optimize isoparaffin reactor. Another recent examples is the methanol to olefins (MTO) reactor. The design of MTO reactor is based on the FCC reactors albeit with quite different hydrodynamics. Unlike FCC reactor, coke deposition in MTO reactor may occur over tens of minutes or more. Lu et al. [111] have developed efficient approach to model MTO reactors by coupling CRE models with the CFD models. With the new approach, simulated values of methanol conversion agreed much better than those obtained with simpler models (like CSTR model). Using this coupled CRE – CFD approach, it was possible to carry out optimization of industrial MTO reactor based on detailed CFD simulations.

Reaction engineering and CFD models are also often used to optimize degree of back-mixing and transport rates for intensifying gas-liquid reactions in bubble columns and reactor – separators. For example, Chaudhari et al. [112] used CFD models to quantify back mixing in bubble columns. The model was then used to design internal

baffles to reduce back mixing for realizing enhanced productivity. Similar sectionalized bubble columns were also used to enhance selectivity of mono-chloroacetic acid in a continuous chlorination bubble column reactor. Lohokare et al. [70] used reaction engineering and CFD models for optimizing external loop gas lift reactor. Darda and Ranade [113] used reaction engineering models for simulating reactive – distillation process for manufacturing isophorone. The operations of isophorone reactor was optimized using the model for realizing enhanced selectivity towards isophorone. Ranade et al. [109] have used computational models to optimize performance of reactor – separator for cases where reactants and products are in vapor phase while reactions occur in liquid phase with homogeneous catalyst. Similar strategies were used to enhance performance of dimethyl carbonate (DMC) reactor using sectionalized horizontal bubble column reactor [25]. In this case, a stripping agent was used to enhance selectivity towards DMC.

Computational models have also been extensively used for intensifying reactions in stirred tank reactors [100,114]. One example is cited here: Patwardhan et al. [115] simulated a large industrial oxidation reactor using CFD. The CFD model gave adequately accurate prediction of the residence time distribution of the industrial scale reactor. The computational model was validated using the measured gas hold-up distribution in the industrial scale reactor (measured using gamma ray tomography). The model was then used to identify bottlenecks of the existing reactor. Several intensification strategies were evolved and computationally investigated. The shortlisted solutions were implemented in the plant which resulted in substantial monetary benefits. Many such examples unfortunately do not get published or even patented.

Computational models have also been used to intensify variety of non-conventional reactors used by sectors other than process industries. For example, Ranade and Gupta [116] have demonstrated use of CFD models to enhance performance of pulverized coal fired boilers. Mujumdar and Ranade [117] have shown how reaction engineering and CFD models can be coupled to enhance performance of cement kilns. Similar models were also used to intensify kilns used for manufacturing hydrofluoric acid (HF). Kuan and Witt [118] have used computational flow models to optimize supersonic quenching of magnesium vapor for developing carbothermal reduction process for magnesium. The model was validated using steam condensation data and applied to study supersonic quenching of magnesium vapor in a laboratory-scale set-up. The model was used for designing and up-scaling processes which eventually resulted CSIRO's MagSonic™ carbothermal magnesium technology.

In their comprehensive review on multiphase reactors Joshi and Nandakumar [119] suggest a paradigm shift by using high fidelity computational models for design and scale up instead of physical modeling and pilot plant testing. In order to achieve this the computational models need to be capable of *a priori* prediction of process performance. Current computational models, especially for multiphase flows, rely on closure models for realistic

1 predictions. Many of the closure models (such as drag) are derived from empirical correlations and careful  
2 validation is required limiting their ability as all-encompassing design tools. The reliability of the computational  
3 models can be improved by using uncertainty quantification approach [120]. Reactions coupled with direct  
4 numerical simulation do away with the closure models, but require enormous computational resources and only  
5 simple and small geometries can be simulated. Nevertheless, a well calibrated and validated CFD model can be  
6 used to examine various designs and operating conditions and can substantially reduce the pilot scale testing  
7 and provide a reliable scale up.

8  
9 There are numerous examples of applying computational models for designing reactors and reactor internals for  
10 intensifying multiphase reactions. Several complex configurations of microreactors have been developed using  
11 these models. The bottleneck in realizing these configurations is manufacturing processes. The manufacturability  
12 of reactors that incorporate new intensified process concepts can have a significant impact on their market and  
13 industry success [121]. The new advances in 3D printing technology [122] can be harnessed to optimize shapes  
14 of process equipment without concerns about manufacturability. This opens up new tools for optimization. For  
15 example, Tao et al. [123] present a hybrid optimization method aiming to design the flow channel shape and  
16 achieve the desired objective. Similar approaches can be used to automate optimization of reactor shapes and  
17 internals and their subsequent manufacturing via 3D printing technology. The technologies for additive  
18 manufacturing are growing at an enormous pace. It is possible to use materials that can withstand high  
19 temperatures and pressures and obtain micron scale resolution. Bikas et al [124] give a critical review of additive  
20 manufacturing methods. Thompson et al [125] provide an overview of trends, opportunities, considerations, and  
21 constraints. Techniques such as stereolithography, metal cold spraying or electrodeposition are compatible with  
22 a large number of catalytic metals and can be used to mass produce tailored reactors. For example, Avril et al.  
23 [126] demonstrate a series of continuous flow hydrogenations of alkenes and carbonyls using a tubular reactor  
24 with 3D printed static mixers. The static mixers are coated with a catalytic metal layer, which can be inserted  
25 into standard stainless steel reactor tubing. Monaghan et al [Monaghan127] report development of 3D printed  
26 lab-on-chip devices that feature integrated optics.

### 27 28 **3.5 Discussion**

29 There may of course be several other ways of intensification which are not touched upon here. We however  
30 believe that the tools and examples discussed here provide useful pointers for wider applications. Here we would  
31 like to discuss few other relevant points related to intensification and share some of the lessons from our  
32 experience.



One of the important points which must be kept in mind while developing intensification strategies for multiphase reactions and reactors is related to process safety considerations. Conflict may arise between intensification and some inherent safety practices. For example, certain intensification technologies require higher energy inputs or to be operated at higher temperatures. The processes may be more complex or call for a more complex control system. These aspects call for due attention to process safety and integrate those considerations while evolving intensification strategies. Intensification of multiphase reactions and reactors may also significantly enhance inherent process safety by reducing inventory of hazardous materials and by realizing enhanced transport rates. Etchells [127,128] have discussed some examples of how process intensification has, or might have, improved safety. Some of the issues related to process safety that need to be considered while devising intensification strategies are also discussed.

At this juncture, it would be useful to re-examine the lessons learnt from our experience of intensification of multiphase reactions and reactors. One of the most important lessons from our experience is; it is extremely important to correctly:

- identify and pose the problem,
- analyze various key issues limiting rate of reactions/ performance of reactor under consideration,
- select an appropriate intensification strategy with due consideration to process safety,
- collect relevant reaction and reactor engineering data; use computational models and develop implementation protocols, and
- implement the strategy in practice

For any engineering discipline, the so-called Occam's razor always provides guidelines for selecting appropriate strategy. Occam's razor can be stated as, 'it is futile to do with more, what can be done with less'. There are many instances where simple intensification strategies may provide elegant and adequate solution. It is, however, important to emphasize here the maxim that says 'one should always try to make things as simple as possible (following the Occam's razor) but not simpler'. It may be necessary to develop more intricate intensification strategies dependent on out of the box thinking. Distinguishing the 'simple' and 'simpler' intensification strategies is often the key for successful implementation. Some of the examples cited here such as using MAGIC tubes are useful to understand this distinction.

The other important lesson is; it is beneficial and more efficient to develop intensification strategies in a hierarchical way. It may be useful to undertake a stage wise development, validation and implementation. Adequate and judicious use of computational models is always helpful in realizing intensification in practice. Advances in software technology, enhanced computing resources and integrated tools encompassing CFD codes

with physical and chemical property data bases to process or reactor simulation tools allow evaluation of changes in the reactor hardware on overall process performance in near future. Such capabilities will significantly influence intensification strategies and practice of tomorrow.

The advances in manufacturing technologies have significantly enhanced realization of complicated reactor geometries. However, uncertainty in scale-up can hinder adoption of new technology and commercialization of efficient processes. Powell [428129] has discussed the challenges in scale up at length from an industrial perspective. The key to a reliable scale up lies in developing advances in computational models that can provide reliable and accurate a priori predictions.

Overall approach of identification of rate limiting step and removing the identified limitations, often leads to sequential steps of intensification of intrinsic chemical reaction rate and intensification of transport rates. If these two ways are explored together, a true synergy can be realized and such synergistic intensification can lead to leapfrogging in productivity. Finally, efficiencies and intensification avenues need to be sought in all areas of a process and not just on reactions and reactors for enhancing sustainability of chemical industry.

#### 4. Summary

The returns or benefits offered by intensification of multiphase reactions and reactors often far exceed the cost of required investments. We have made an attempt to provide some insights on strategies for and some examples of intensification of multiphase reactions and reactors. Intensification may be realized by using basic ideas on chemistry and catalysis to making modifications in existing reactor designs or operating protocols. The discussion will hopefully help to select appropriate strategy for intensification. Overall methodology of achieving objectives of performance enhancement is discussed with the help of examples. An attempt is made to evolve general guidelines, which may be useful for solving practical intensification projects. It is our experience that every time when our intensification efforts led to some benefits in practice; it strengthened our interest and encouraged us to explore further intensification opportunities.

Adequate attention to key issues mentioned in here and creative use of strategies will make significant contributions in enhancing chemical reactor engineering. Field of intensification of multiphase reactions and reactors is continuously evolving and being continuously updated. New advances may be assimilated using the framework discussed here. We hope that this will further stimulate development of intensification strategies for multiphase reactions and reactors.

## Acknowledgements

We had contacted numerous researchers working in the area of intensification of multiphase reactions and reactors. We are grateful to many of these researchers who provided their feedback and suggested excellent intensification examples to us.

## References:

- [1] Doraiswamy LK, Sharma MM. *Heterogeneous reactions: Analysis, Examples and Reactor design. Vol. 1 and 2*; Wiley **1984**
- [2] Sharma, M.M. Intensification of heterogeneous reactions: theory and practice, *Proceedings of Indian National Science Academy*, **1986** **52** A (2), 449-475.
- [3] Reese, M.; Marquart, C.; Malmali, M.; Wagner, K.; Buchanan, E.; McCormick, A.; Cussler, E. L. Performance of a Small-Scale Haber Process. *Ind. Eng. Chem. Res.* 2016, **55** (13), 3742.
- [4] Stankiewicz AI, Moulijn JA. Process intensification: transforming chemical engineering. *Chemical Engineering Progress*. **2000** **96**(1):22-34.
- [5] Ranade, V. V., Sharma, M. K. & Kulkarni, A. A. CRE for MAGIC (modular, agile, intensified & continuous) processes, *Chemical Engineering Journal*. **2015** **278**, 458-468.
- [6] Doraiswamy LK. *Organic Synthesis Engineering*. Oxford University Press. **2001**.
- [7] Joshi, S.S., and V.V. Ranade. *Industrial Catalytic Processes for Fine and Specialty Chemicals*. Elsevier Science, 2016.
- [8] Pragt JJ, Jongmans MT, Bargeman G, Schuur B, Aaldering JT, Nieuwhof MR, Kiss AA, De Haan AB, Rodriguez AL, Van Strien CJ (Inventors); Akzo Nobel Chemicals International BV (Assignee). Process for separating monochloroacetic acid and dichloroacetic acid via extractive distillation using an organic solvent. *United States patent US 9,187,400*. **2015**.
- [9] Garkhedkar AM, Shingote SK, Rane VH, Kelkar AA, Ranade VV. Intensifying Hydrogenation of Cinnamaldehyde to Cinnamyl Alcohol: Catalyst, Solvent and Operating Conditions. *Indian Chemical Engineer*. **2015** **57**(3-4):219-39.
- [10] Talwalkar S, Thotla S, Sundmacher K, Mahajani S. Simultaneous Hydrogenation and Isomerization of Diisobutylenes over Pd-Doped Ion-Exchange Resin Catalyst. *Ind. Eng. Chem. Res.* **2009** **48**(24):10857-63.
- [11] Mallat, T., E. Orglmeister, and A. Baiker, Asymmetric Catalysis at Chiral Metal Surfaces, *Chem. Rev.* 2007, **107**, 4863-4890
- [12] Jin X, Dang L, Lohrman J, Subramaniam B, Ren S, Chaudhari RV. Lattice-matched bimetallic CuPd-graphene nanocatalysts for facile conversion of biomass-derived polyols to chemicals. *Acs Nano*. **2013** **7**(2):1309-16.
- [13] Jin X, Zhao M, Shen J, Yan W, He L, Thapa PS, Ren S, Subramaniam B, Chaudhari RV. Exceptional performance of bimetallic Pt 1 Cu 3/TiO 2 nanocatalysts for oxidation of gluconic acid and glucose with O 2 to glucaric acid. *Journal of Catalysis*. **2015** **330**:323-9.

- [14] Gadge, ST, Bhanage, BM, 2016, "Selection of Reaction Media" in Industrial Catalytic Processes for Fine and Specialty Chemicals, Ed. Joshi and Ranade, pp 221
- [15] Mehra A. Intensification of multiphase reactions through the use of a microphase — I. Theoretical. *Chem. Eng. Sci.* **1988** 43(4):899-912.
- [16] Mehra A, Pandit A, Sharma MM. Intensification of multiphase reactions through the use of a microphase— II. Experimental. *Chem. Eng. Sci.* **1988** Jan 1;43(4):913-27.
- [17] Behr A, Henze G, Johnen L, Awungacha C. Advances in thermomorphic liquid/liquid recycling of homogeneous transition metal catalysts. *J Mol Catal A Chem.* 2008;285(1–2):20–28.
- [18] Dreimann, J. M., H. Warmeling, J. N. Weimann, K. K€unnemann, A. Behr, and A. J. Vorholt, Increasing Selectivity of the Hydroformylation in a Miniplant: Catalyst, Solvent, and Olefin Recycle in Two Loops, 2016, AIChE Journal, 62 (12), 4377-4383.
- [19] Deshpande K, Dixit RS, (Inventors); Dow Global Technologies Llc, (Assignee). Olefin-based polymers and dispersion polymerizations. United States patent application *US 13/991,836*. **2011**.
- [20] Ranade, V.V., S.S. Joshi and C.V. Rode , Improved temperature control in a single step nitrobenzene hydrogenation process for paraminophenol by use of inert solvent, NCL Internal report/ NCL invention disclosure. 2015
- [21] James SL, Adams CJ, Bolm C, Braga D, Collier P, Frišćić T, Grepioni F, Harris KD, Hyett G, Jones W, Krebs A. Mechanochemistry: opportunities for new and cleaner synthesis. *Chemical Society Reviews.* **2012** 41(1):413-47.
- [22] Crawford, D. E., L. A. Wright, S. L. James and A. P. Abbott, Efficient continuous synthesis of high purity deep eutectic solvents by twin screw extrusion, *Chem. Commun.*, 2016, 52, 4215-4218
- [23] Crawford, D.E., J. Casaban, R. Haydon, N. Giri, T. McNally and S. L. James, Synthesis by extrusion: continuous, large-scale preparation of MOFs using little or no solvent, *Chem. Sci.*, 2015, 6, 1645 - 1649
- [24] Reddy B, Bhat R, Agrawal A, Patidar P, Mahajani S. Comparison of reactive chromatography and reactive distillation for the synthesis of C1–C4 acetates. *Chemical Engineering and Processing: Process Intensification.* **2015** 95:17-25.
- [25] Ranade, V.V., A.A. Kelkar, V.H. Rane, S.S. Shingote and L.S. Roy (2014) Synthesis of methyl carbamate and dimethyl carbonate (dmc) in presence of stripping with inert gas or superheated vapors and a reactor for the same, WO 2014072803 A1
- [26] Ranade, V.V. and D.R. Mote (2016), Reaction Engineering of Urea Alcoholysis, AIChE Annual Meeting, Paper 375b.
- [27] Fernandez E, Helmi A, Coenen K, Melendez J, Viviente JL, Tanaka DA, van Sint Annaland M, Gallucci F. Development of thin Pd–Ag supported membranes for fluidized bed membrane reactors including WGS related gases. *International journal of hydrogen energy.* **2015** 40(8):3506-19.
- [28] Giorno L., and E. Drioli, Biocatalytic membrane reactors: applications and perspectives, *TIBTECH* AUGUST 2000 (Vol. 18), 339-349.

- [29] Bhatia, S. W. S. Long, A. H. Kamaruddin, Enzymatic membrane reactor for the kinetic resolution of racemic ibuprofen ester: modeling and experimental studies, *Chemical Engineering Science* 59 (2004) 5061 – 5068
- [30] Atlas JA, Carlberg PJ, Dixit RS, Drake RM, Tirtowidjojo D, West DH, Worley WG, Young TC, (Inventors); Dow Global Technologies LLC, (Assignee). Epoxy resin production. United States patent application *US 14/365,753*. **2012**.
- [31] Hessel, V., H. Löwe, F. Schönfeld, Micromixers—a review on passive and active mixing principles, *Chemical Engineering Science* 60 (2005) 2479 – 2501
- [32] Falk, L., J.-M. Commenge, Performance comparison of micromixers, *Chemical Engineering Science*. 65 (2010) 405—411
- [33] Boroun S, Larachi F. Enhancing liquid micromixing using low-frequency rotating nanoparticles. *AIChE Journal*. **2016** Aug 1.
- [34] Boroun, S., & Larachi, F. (2016). Role of magnetic nanoparticles in mixing, transport phenomena and reaction engineering—challenges and opportunities. *Current Opinion in Chemical Engineering*, 13, 91-99.
- [35] Kulkarni A.A. and V.V. Ranade (2014) Flow reactor with pinched pipe sections for mixing and heat transfer, WO 2014/167506A1
- [36] Hasabnis NS, Totlani KA, Ranade VV. Heat transfer and mixing in flow through pinched pipe. *The Canadian Journal of Chemical Engineering*. **2015** 93(10):1860-8.
- [37] Hasabnis NS, Ranade VV. Flow and Heat Transfer in a Pinched Helical Coil. *Indian Chemical Engineer*. **2015** 57(1):1-4.
- [38] Sharma, M.K., S. B. Potdar and A.A. Kulkarni (2017) Pinched tube flow reactor: Hydrodynamics and suitability for exothermic multiphase reactions, *AIChE Journal*, **63**, 358–365.
- [39] Joshi RA, Joshi RR, Tibhe J, Nivangune NT, Kulkarni AA. Continuous flow synthesis of  $\beta$ -amino  $\alpha$ ,  $\beta$ -unsaturated esters in aqueous medium. *Green Processing and Synthesis*. **2012** 1(2):205-10.
- [40] Andersson R, Andersson B, Chopard F, Norén T. Development of a multi-scale simulation method for design of novel multiphase reactors. *Chem Eng Sci*. **2004** 59(22):4911-7.
- [41] Stankiewicz AI. Process intensification in in-line monolithic reactor, *Chemical Engineering Science* 56 **2001** 359-364
- [42] Pollington SD, Enache DI, Landon P, Meenakshisundaram S, Dimitratos N, Wagland A, Hutchings GJ, Stitt EH. Enhanced selective glycerol oxidation in multiphase structured reactors. *Catalysis Today*. **2009** 145(1):169-75.
- [43] Pennemann, H., G Kolb, "Review: Microstructured reactors as efficient tool for the operation of selective oxidation reactions", *Catalysis Today* 278 (2016) 3–21
- [44] Faridkhou, A., J-N. Tourvieille, , F. Larachi, "Reactions, hydrodynamics and mass transfer in micro-packed beds— Overview and new mass transfer data", *Chemical Engineering and Processing* 110 (2016) 80–96

- [45] Azizi F, Al Taweel AM. Mass Transfer in an Energy-Efficient High-Intensity Gas–Liquid Contactor. *Ind. Eng. Chem. Res.* **2015** 54(46):11635-52.
- [46] Al Taweel, A. M.; Azizi, F.; Sirijeerachai, G. Static Mixers: Effective Means for Intensifying Mass Transfer Limited Reactions. *Chem. Eng. Process.* 2013, 72, 51.
- [47] Jain D, Lau YM, Kuipers JA, Deen NG. Discrete bubble modeling for a micro-structured bubble column. *Chem. Eng. Sci.* **2013** 100:496-505.
- [48] Jain D, Kuipers JA, Deen NG. Numerical modeling of carbon dioxide chemisorption in sodium hydroxide solution in a micro-structured bubble column. *Chem. Eng. Sci.* **2015** 137:685-96.
- [49] Enache DI, Thiam W, Dumas D, Ellwood S, Hutchings GJ, Taylor SH, Hawker S, Stitt EH. Intensification of the solvent-free catalytic hydroformylation of cyclododecatriene: Comparison of a stirred batch reactor and a heat-exchange reactor. *Catalysis Today.* **2007** Oct 15; 128(1):18-25.
- [50] Yap SK, Yuan Y, Zheng L, Wong WK, Zhang J, Yan N, Khan SA. Rapid nanoparticle-catalyzed hydrogenations in triphasic millireactors with facile catalyst recovery. *Green Chemistry.* **2014** 16(11):4654-8.
- [51] Yap S, Yuan Y, Zheng L, Wong W, Yan N, Khan S. Triphasic Segmented Flow Millireactors for Rapid Nanoparticle-Catalyzed Gas–Liquid Reactions—Hydrodynamic Studies and Reactor Modeling. *Journal of Flow Chemistry.* **2014** 4(4):200-5.
- [52] Sharma Y, Joshi RA, Kulkarni AA. Continuous-Flow Nitration of o-Xylene: Effect of Nitrating Agent and Feasibility of Tubular Reactors for Scale-Up. *Org. Process Res. Dev.* **2015** 19(9):1138-47.
- [53] Shukla, C. A., A. A. Kulkarni and V. V. Ranade, Selectivity Engineering of Diazotization Reaction in Continuous Flow Reactor, Reaction Chemistry and Engineering, 2016.
- [54] Tonkovich, A. L., S. Deshmukh, Process intensification of multiphase catalytic reactions, 2016, Private Communications
- [55] Ahmed B, Barrow D, Wirth T. Enhancement of reaction rates by segmented fluid flow in capillary scale reactors. *Advanced Synthesis & Catalysis.* **2006** 348(9):1043-8.
- [56] Cambié D, Bottecchia C, Straathof NJ, Hessel V, Noël T. Applications of Continuous-Flow Photochemistry in Organic Synthesis, Material Science, and Water Treatment. *Chemical reviews.* **2016**.
- [57] Damm M, Gutmann B, Kappe CO. Continuous-Flow Synthesis of Adipic Acid from Cyclohexene Using Hydrogen Peroxide in High-Temperature Explosive Regimes. *ChemSusChem.* **2013** 6(6):978-82.
- [58] Gutmann B, Elsner P, Cox DP, Weigl U, Roberge DM, Kappe CO. Toward the Synthesis of Noroxymorphone via Aerobic Palladium-Catalyzed Continuous Flow N-Demethylation Strategies. *ACS Sustainable Chemistry & Engineering.* **2016**.
- [59] Gemoets HP, Su Y, Shang M, Hessel V, Luque R, Noël T. Liquid phase oxidation chemistry in continuous-flow microreactors. *Chemical Society Reviews.* **2016** 45(1):83-117.

- [60] Erdmann N, Su Y, Bosmans B, Hessel V, Noël T. Palladium-catalyzed aerobic oxidative coupling of o-xylene in flow: a safe and scalable protocol for cross-dehydrogenative coupling. *Org. Process Res. Dev.* **2016** 20(4):831-5.
- [61] Schnider, C., D. Roberge, M. Gottsponer, A. Klein, T. Gruetzner and M. Bittel (2015), Method for preparation of imidodisulfuryl compounds, WO2015/004220 A1
- [62] Peer M, Weeranoppanant N, Adamo A, Zhang Y, Jensen KF. Biphasic Catalytic Hydrogen Peroxide Oxidation of Alcohols in Flow: Scale-up and Extraction. *Org. Process Res. Dev.* **2016** 20(9):1677-85.
- [63] Jeong GY, Singh AK, Sharma S, Gyak KW, Maurya RA, Kim DP. One-flow syntheses of diverse heterocyclic furan chemicals directly from fructose via tandem transformation platform. *NPG Asia Materials.* **2015** 7(4):e173.
- [64] Heitmann D. Continuous and Intensified Laboratory Process Development at Clariant. *Chemical Engineering & Technology.* **2016** 39(11):1993-5.
- [65] Singh AK, Ko DH, Vishwakarma NK, Jang S, Min KI, Kim DP. Micro-total envelope system with silicon nanowire separator for safe carcinogenic chemistry. *Nature communications.* **2016** Feb 26;7.
- [66] Movsisyan M, Delbeke EI, Berton JK, Battilocchio C, Ley SV, Stevens CV. Taming hazardous chemistry by continuous flow technology. *Chemical Society Reviews.* **2016**; 45(18):4892-928.
- [67] Karande R, Schmid A, Buehler K. Applications of multiphasic microreactors for biocatalytic reactions. *Org. Process Res. Dev.* **2016** 20(2):361-70.
- [68] van Alsten JG, Jorgensen ML, am Ende DJ. Hydrogenation of a pharmaceutical intermediate by a continuous stirred tank reactor system. *Org. Process Res. Dev.* **2009** 13(3):629-33.
- [69] Rode, C.V., S.S. Joshi and V.V. Ranade, A continuous process for paraminophenol, Indian Patent filing, CSIR, 2015.
- [70] Lohokare SR, Bhusare VH, Joshi JB. Process Intensification: A Case Study. *Indian Chemical Engineer.* **2015** 57(3-4):202-18.
- [71] Otterstätter R, Zanthoff HW, Klemm E. Three-Phase Heterogeneously Catalyzed Oxidative Esterification—Relevance of Oxygen Mass Transport. *Chemical Engineering & Technology.* **2016** 39(11):2029-34.
- [72] Tan J, Zhang JS, Lu YC, Xu JH, Luo GS. Process intensification of catalytic hydrogenation of ethylantraquinone with gas-liquid microdispersion. *AIChE Journal.* **2012** 58(5):1326-35.
- [73] Subramaniam B, Busch DH, Niu F, (Inventors); University Of Kansas, (Assignee). Spray process for selective oxidation. United States patent *US 9,238,608.* **2016.**
- [74] Grasemann M, Renken A, Kashid M, Kiwi-Minsker L. A novel compact reactor for three-phase hydrogenations. *Chemical Engineering Science.* **2010** 65(1):364-71.
- [75] Rehm TH, Gros S, Löb P and Renken A. Photonic contacting of gas-liquid phases in a falling film microreactor for continuous-flow photochemical catalysis with visible light, *Reaction Chemistry & Engineering*, **2016** DOI: 10.1039/c6re00169f

- [76] Greenwald E, Gordon JM, Zarmi Y. Physics of ultra-high bioproductivity in algal photobioreactors. *Applied Physics Letters*. **2012** 100(14):143703.
- [77] Visscher F, Van der Schaaf J, Nijhuis TA, Schouten JC. Rotating reactors—A review. *Chemical Engineering Research and Design*. **2013** 91(10):1923-40.
- [78] Aoune, A.; Ramshaw, C. *Int. J. Heat Mass Transfer* 1999, 42, 2543–2556
- [79] Meeuwse M, van der Schaaf J, Schouten JC. Mass Transfer in a Rotor–Stator Spinning Disk Reactor with Co-feeding of Gas and Liquid. *Ind. Eng. Chem. Res.* **2009** 49(4):1605-10.
- [80] Subramanian K, Winkler M, Härting HU, Schubert M. Prediction of Flow Patterns of Rotating Inclined Reactors by Using a Modified Permeability Approach. *Chemical Engineering & Technology* **2016** 39(11):2077-86.
- [81] Härting, Hans-Ulrich, et al. "A novel inclined rotating tubular fixed bed reactor concept for enhancement of reaction rates and adjustment of flow regimes." *Chemical Engineering Journal* 281 (2015): 931-944.
- [82] Motamed Dashliborun, Amir, et al. "Process intensification of gas–liquid downflow and upflow packed beds by a new low-shear rotating reactor concept." *AIChE Journal* 63.1 (2017): 283-294.
- [83] Dietrich W, Anadon L, Sederman A, Gladden L, Agar D. Simulation studies on the performance enhancement in periodically operated trickle-bed reactors based on experimental local liquid distribution measurements. *Ind. Eng. Chem. Res.* **2011** 51(4):1672-9.
- [84] Gelhausen, M. G., S. Yang, M. Cegla, D. W. Agar. Cyclic mass transport phenomena in a novel reactor for gas-liquid-solid contacting, *AIChE Journal*, **2016**, DOI 10.1002/aic.15532
- [85] Nikolić D, Seidel-Morgenstern A, Petkovska M. Periodic Operation with Modulation of Inlet Concentration and Flow Rate. Part I: Nonisothermal Continuous Stirred-Tank Reactor. *Chemical Engineering & Technology*. **2016** 39(11):2020-8.
- [86] Hamidipour M, Larachi F. Modulation of suspension electrical conductivity to counter fines plugging in trickle-bed reactors. *AIChE Journal*. **2011** 57(7):1829-39.
- [87] Liedtke AK, Scheiff F, Bornette F, Philippe R, Agar DW, de Bellefon C. Liquid–Solid Mass Transfer for Microchannel Suspension Catalysis in Gas–Liquid and Liquid–Liquid Segmented Flow. *Ind. Eng. Chem. Res.* **2015** 54(17):4699-708.
- [88] Losey MW, Schmidt MA, Jensen KF. Microfabricated multiphase packed-bed reactors: characterization of mass transfer and reactions. *Ind. Eng. Chem. Res.* **2001** 40(12):2555-62.
- [89] Stankiewicz, A. "Energy matters: alternative sources and forms of energy for intensification of chemical and biochemical processes." *Chemical Engineering Research and Design* 84, no. 7 (2006): 511-521.
- [90] Stefanidis, Georgios, and Andrzej Stankiewicz, eds. *Alternative Energy Sources for Green Chemistry*. Vol. 47. Royal Society of Chemistry, 2016.
- [91] Kiss, A. A. (2016). *Process Intensification: Industrial Applications*. In *Process Intensification in Chemical Engineering* (pp. 221-260). Springer International Publishing.



- [92] Ramírez, A., Hueso, J. L., Mallada, R., & Santamaría, J. (2016). Ethylene epoxidation in microwave heated structured reactors. *Catalysis Today*, 273, 99-105.
- [93] Benaskar, F., A. Ben-Abdelmoumen, N.G. Patil, E.V. Rebrov, J. Meuldijk, L.A. Hulshof, V. Hessel, U. Krtischil, J.C. Schouten, Cost analysis for a continuously operated fine chemicals production plant at 10 kg/day using a combination of microprocessing and microwave heating, *J. Flow Chem.* 1 (2011) 74–89.
- [94] Cravotto G, Borretto E, Oliverio M, Procopio A, Penoni A. Organic reactions in water or biphasic aqueous systems under sonochemical conditions. A review on catalytic effects. *Catalysis Communications*. **2015** 63:2-9.
- [95] Chakma S, Moholkar VS. Sonochemical synthesis of mesoporous  $ZrFe_2O_5$  and its application for degradation of recalcitrant pollutants. *RSC Advances*. **2015** 5(66):53529-42.
- [96] Gaikwad ND, Gogate PR. Synthesis and application of carbon based heterogeneous catalysts for ultrasound assisted biodiesel production. *Green Processing and Synthesis*. **2015** 4(1):17-30.
- [97] Dubey SM, Gogate PR. Ultrasound Assisted Synthesis of 4-Benzyloxy-3-methoxybenzaldehyde by Selective O-Alkylation of Vanillin with Benzyl Chloride in the Presence of Tetrabutylammonium Bromide. *Ind. Eng. Chem. Res.* **2014** 53(19):7979-85.
- [98] Ranade, V. V., A. A. Kulkarni, and V. M. Bhandari. "Vortex diodes as effluent treatment devices." United States Patent 9422952, 2016.
- [99] Botte, G.G. (2014), Electrochemical Manufacturing in the Chemical Industry, The Electrochemical Society Interface, Fall 2014, 49-55.
- [100] Ranade, Vivek V. Computational Flow Modeling for Chemical Reactor Engineering. Vol. 5. Academic Press, 2002.
- [101] Hou B, Huang Y, Wang X, Yang X, Duan H, Zhang T. Optimization and simulation of the Sabatier reaction process in a packed bed. *AIChE Journal*. **2016**.
- [102] Girotra, K. S. & Ranade, V. V. Regeneration protocols for fixed bed reactors deactivated by coke, *Chemical Engineering Communications*. 1999 171, p. 55-76.
- [103] Ranade, V.V. (2002) At the heart of the process- reactor engineering, *Chemical Engineering*, **109**, 8, 84-85, 2002
- [104] Dixon AG, Boudreau J, Rocheleau A, Troupel A, Taskin ME, Nijemeisland M, Stitt EH. Flow, transport, and reaction interactions in shaped cylindrical particles for steam methane reforming, *Ind Eng Chem Res.* 2012; **51**, 15839–15854.
- [105] Wehinger G. D., M. Kraume, V. Berg and O. Korup, K. Mette and R. Schlögl, M. Behrens and R Horn, Investigating Dry Reforming of Methane with Spatial Reactor Profiles and Particle-Resolved CFD Simulations, 2016, *AIChE Journal*, 62 (12), 4436-4452.
- [106] Karthik, G.M. and V.V. Buwa (2017) Effect of particle shape on fluid flow and heat transfer for methane steam reforming reactions in a packed bed, *AIChE Journal*, **63**, 366–377.

- [107] Ranade, V.V. (1998) Multiphase reactor engineering, *Speedup Journal*, **12**, 26 - 33, 1998
- [108] Nayak, S. V., Joshi, S. L. & Ranade, V. V. Modeling of vaporization and cracking of liquid oil injected in a gas-solid riser, *Chem. Eng. Sci.* **2005** 60, 22, p. 6049-6066.
- [109] Ranade, V. V., Pushing the limits of existing reactor hardware using computational flow modelling: A case of oxyhydrochlorination reactor, *Current Science*. **1999** 77, 10, p. 1303-1310.
- [110] Lu B, Wang W, Li J, Wang X, Gao S, Lu W, Xu Y, Long J. Multi-scale CFD simulation of gas–solid flow in MIP reactors with a structure-dependent drag model. *Chem. Eng. Sci.* **2007** 62(18):5487-94.
- [111] Lu B, Luo H, Li H, Wang W, Ye M, Liu Z, Li J. Speeding up CFD simulation of fluidized bed reactor for MTO by coupling CRE model. *Chem. Eng. Sci.* **2016** 143:341-50.
- [112] Chaudhari, A. S., Rampure, M. R., Ranade, V. V., Jaganathan, R. & Chaudhari, R. V., Modeling of bubble column slurry reactor for reductive alkylation of p-phenylenediamine, *Chem. Eng. Sci.* **2008** 62, 24, p. 7290-7304
- [113] Darda, P. J. & Ranade, V. V. Isophorone reactor: Modelling and performance enhancement, *Chemical Engineering Journal*. **2012**, 207, 349-367.
- [114] Khopkar, A. R. & Ranade, V. V. Stirred Vessels: Computational Modeling of Multiphase Flows and Mixing, *Chemical Engineering in the Pharmaceutical Industry: R&D to Manufacturing*. John Wiley and Sons Ltd, p. 269-297 **2010**.
- [115] Patwardhan AW, Joshi JB, Fotedar S, Mathew T. Optimization of gas–liquid reactor using computational fluid dynamics. *Chem. Eng. Sci.* **2005** 60(11):3081-9.
- [116] Ranade, Vivek V., and Devkumar F. Gupta. Computational Modeling of Pulverized Coal Fired Boilers. CRC Press, 2014.
- [117] Mujumdar, K. S. & Ranade, V. V. CFD modeling of rotary cement kilns, *Asia-Pacific Journal of Chemical Engineering*. **2008** 3, 2, 106-118.
- [118] Kuan BT, Witt PJ. Modelling supersonic quenching of magnesium vapour in a Laval nozzle. *Chem. Eng. Sci.* **2013** 87:23-39.
- [119] Joshi, J.B., Nandakumar, K., 2015. Computational modeling of multiphase reactors. *Annu. Rev. Chem. Biomol. Eng.* 6, 347–378.
- [120] Gel, A., Garg, R., Tong, C., Shahnam, C., Guenther, C, M., 2013. Applying uncertainty quantification to multiphase flow computational fluid dynamics. *Powder Technol.* 242, 27–39.
- [121] DOE (U. S. Department of Energy), 2015. Quadrennial Technology Review 2015, Process Intensification, Chapter 6: Innovating Clean Energy Technologies in Advanced Manufacturing, Technology Assessments.
- [122] Wimpenny, David Ian, Pulak M. Pandey, and L. Jyothish Kumar. "Advances in 3D Printing & Additive Manufacturing Technologies." (2016).
- [123] Tao, M, G. Kai, H. Zheqing, L. Hui and L. Chunjiang (2016) A hybrid optimization method to design shapes of three-dimensional flow channels, *Chemical Engineering Research and Design*, **114** ( 2 0 1 6 ) 190–201

- [124] Bikas, H., P. Stavropoulos, and G. Chrysosouris. "Additive manufacturing methods and modelling approaches: a critical review." *The International Journal of Advanced Manufacturing Technology* 83.1-4 (2016): 389-405.
- [125] Thompson, Mary Kathryn, et al. "Design for Additive Manufacturing: Trends, opportunities, considerations, and constraints." *CIRP Annals-Manufacturing Technology* 65.2 (2016): 737-760.
- [126] Avril, A., et al. "Continuous flow hydrogenations using novel catalytic static mixers inside a tubular reactor." *Reaction Chemistry & Engineering* (2017).
- [127] Monaghan, T. M. J. Harding, R. A. Harris, R. J. Friel, and S. Christie, "Customisable 3D printed microfluidics for integrated analysis and optimisation.", *Lab on a Chip*, **16**, no. 17 (2016): 3362-3373
- [127128] Etchells JC. Process Intensification: Safety Pros and Cons. *Process Safety and Environmental Protection*. **2005** 83(2):85-9.
- [128129] Powell, Joseph B. "Application of multiphase reaction engineering and process intensification to the challenges of sustainable future energy and chemicals." *Chemical Engineering Science* 157 (2017): 15-25.
- [129130] van Hasselt B.W., H.P.A. Calis, S.T. Sie, C.M. van den Bleek (2001) Gas-liquid mass transfer characteristics of the three-levels-of-porosity reactor, *Chemical Engineering Science*, Volume 56, Issue 2, January 2001, Pages 531-536

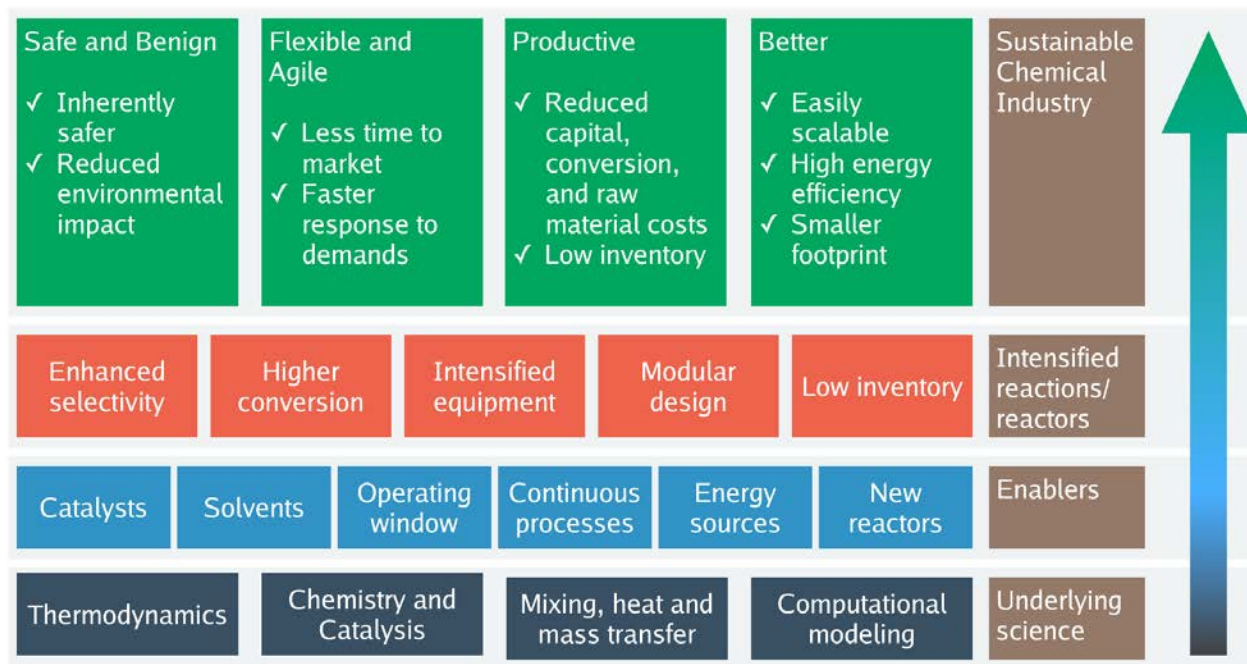
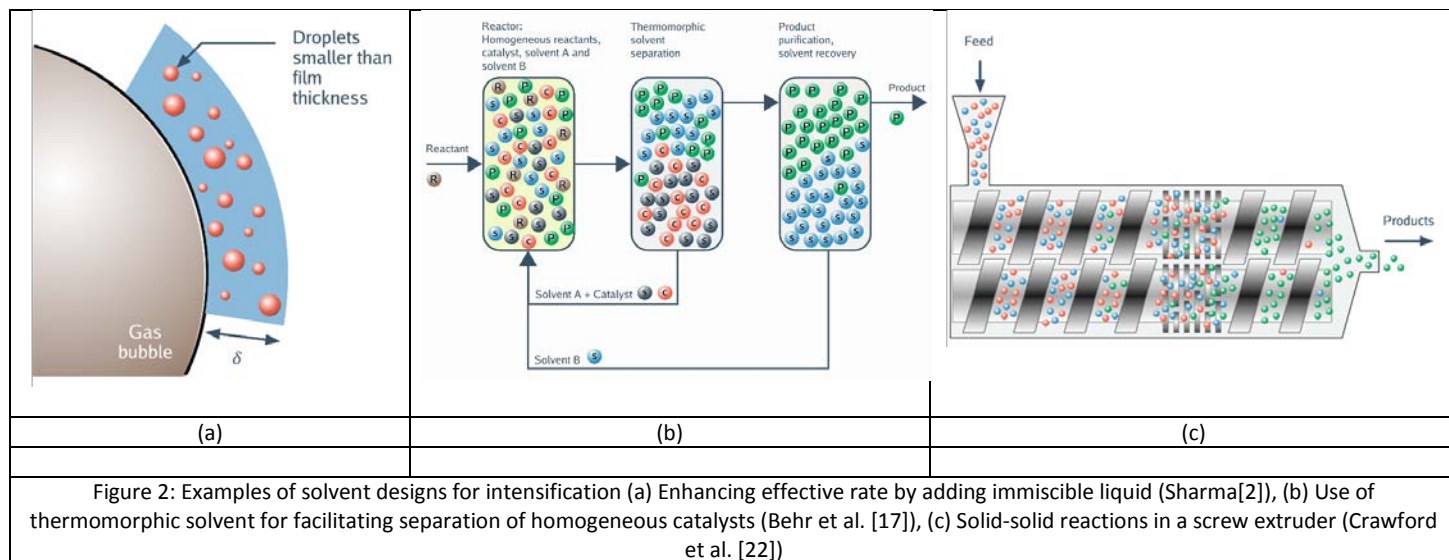
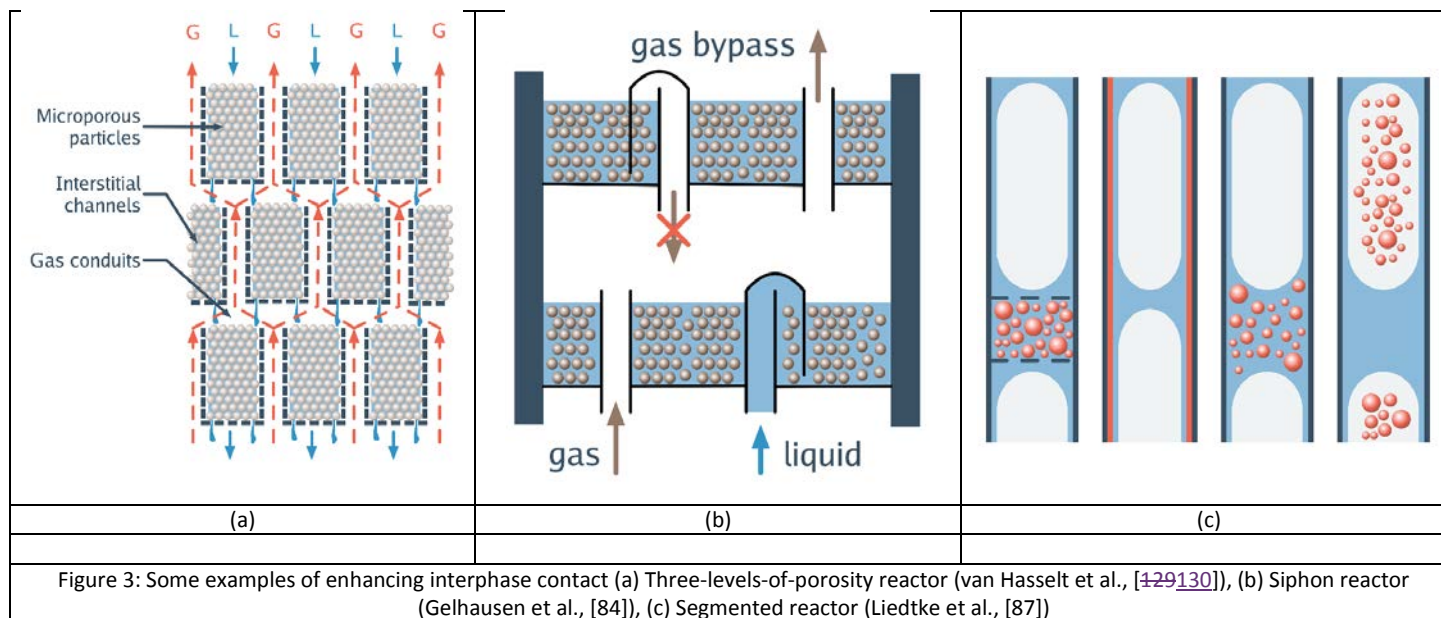
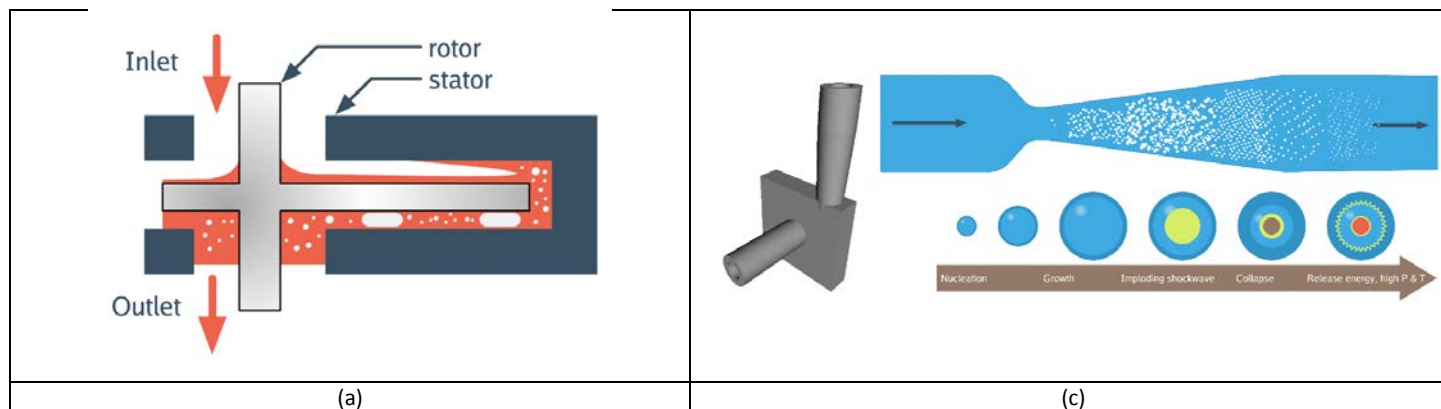
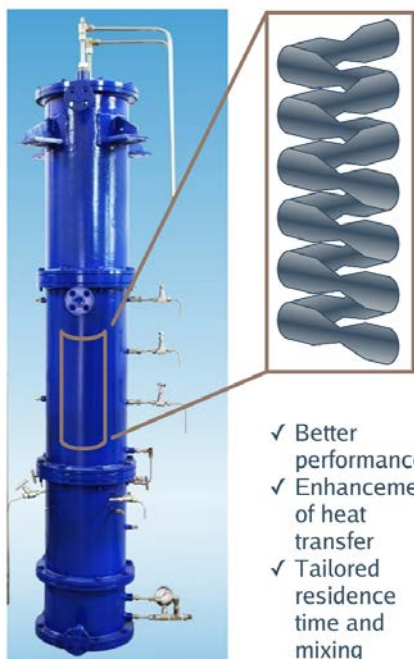


Figure 1: Intensification of multiphase reactions and reactors



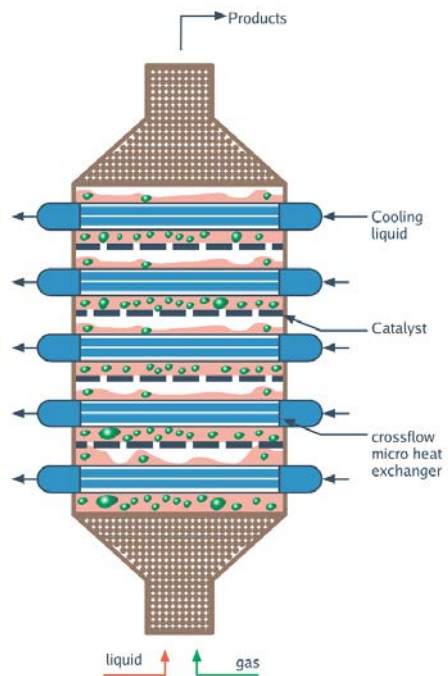






- ✓ Better performance
- ✓ Enhancement of heat transfer
- ✓ Tailored residence time and mixing

(b)



(d)

Figure 4: Some examples of intensified reactors (a) Rotor-stator spinning disk (Visscher et al., [77]), (b) Pinched tube reactor (Sharma et al., [38]), (c) Cavitation reactor (Ranade et al., [98]), (d) Structured bubble column reactor (Grasemann et al., [74])

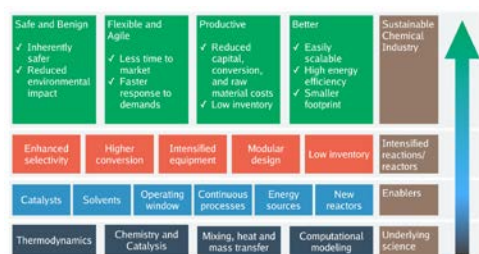


## For table of contents use only

Title: Intensifying Multiphase Reactions and Reactors: Strategies & Examples

Authors: Ranjeet P. Utikar and Vivek V. Ranade

Synopsis: The interplay between various factors affecting intensification of multiphase reactions and reactors for sustainable process industry. This note discusses various strategies for intensifying multiphase reactions and reactors for sustainable production.





Dr. Ranjeet Utikar is senior lecturer at Curtin University, Australia. Dr Utikar's work in the area of industrial flow modelling has resulted into direct measurable benefits to the chemical, environmental and auto industry and has been incorporated into proprietary commercial modelling and design systems. He has worked with several multinationals on modelling, troubleshooting, optimisation of various unit operations as well as process development. Dr. Utikar has previously worked at CSIR-NCL, University of Twente, and DSM Netherlands. He is also an entrepreneur and is a founder of two companies:

Tridiagonal Solutions; Vivira Process Technologies Pvt. Ltd.



Dr. Vivek Ranade is a Professor of Chemical Engineering at the School of Chemistry and Chemical Engineering of Queen's University Belfast. His research focus is on sustainable energy, water and fine & specialty chemicals. Earlier led chemical engineering and process development at National Chemical Laboratory, Pune. Contributed significantly to chemical engineering science and practice. Developed performance enhancement solutions, software products and fluidic devices for variety of applications which are commercialized. Developed new insights and methodologies for MAGIC (modular, agile, intensified & continuous) processes & plants. He also worked at TUDelft, University of Twente and ETH

Zurich. Co-founded two technology companies: Tridiagonal Solutions and VIVIRA Process Technologies.